NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING SAME

RELATED APPLICATIONS

This application claims priority from USSN 60/256,635 filed December 18, 2000 (Cura-524); USSN 60/259,743 filed January 4, 2001 (Cura-524 A); USSN 60/299,327 filed June 19, 2001 (Cura-524 A1); USSN 60/261,498 filed January 12, 2001 (Cura-524 B); USSN 60/263,689 filed January 24, 2001 (Cura-524 C); USSN 60/267,464 filed February 8, 2001 (Cura-524 D); USSN 60/271,021 filed February 22, 2001 (Cura-524 E); USSN 60/275,946 filed March 14, 2001 (Cura-524 F); USSN 60/278,150 filed March 23, 2001 (Cura 524 G); USSN 60/285,718 filed April 23, 2001 (Cura-524 H); USSN 60/312,902 filed August 16, 2001 (Cura-524 I); 60/257,876 filed December 21, 2000 (Cura-527); USSN 60/260,718 filed January 10, 2001 (Cura-527 A); and USSN 60/284,591 filed April 18, 2001 (Cura-527 B), each of which is incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

The invention generally relates to nucleic acids and polypeptides. More particularly, the invention relates to nucleic acids encoding novel G-protein coupled receptor (GPCR) polypeptides, as well as vectors, host cells, antibodies, and recombinant methods for producing these nucleic acids and polypeptides.

SUMMARY OF THE INVENTION

The invention is based in part upon the discovery of nucleic acid sequences encoding novel polypeptides. These nucleic acids and polypeptides, as well as derivatives, homologs, analogs and fragments thereof, will hereinafter be collectively designated as "GPCRX" nucleic acid or polypeptide sequences.

In one aspect, the invention provides an isolated GPCRX nucleic acid molecule encoding a GPCRX polypeptide that includes a nucleic acid sequence that has identity to the nucleic acids disclosed in SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159,

161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199. In some embodiments, the GPCRX nucleic acid molecule will hybridize under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule that includes a protein-coding sequence of a GPCRX nucleic acid sequence. The invention also

5   includes an isolated nucleic acid that encodes a GPCRX polypeptide, or a fragment, homolog, analog or derivative thereof. For example, the nucleic acid can encode a polypeptide at least 80% identical to a polypeptide comprising the amino acid sequences of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104,

10   106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200. The nucleic acid can be, for example, a genomic DNA fragment or a cDNA molecule that includes the nucleic acid sequence of any of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33,

15   35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199. Also included in the invention is an oligonucleotide, *e.g.*, an oligonucleotide which

20   includes at least 6 contiguous nucleotides of a GPCRX nucleic acid (*e.g.*, SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175,

25   177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199) or a complement of said oligonucleotide.

       Also included in the invention are substantially purified GPCRX polypeptides (*e.g.*, SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94,

30   96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200). In

certain embodiments, the GPCRX polypeptides include an amino acid sequence that is substantially identical to the amino acid sequence of a huma GPCRX polypeptide.

The invention also features antibodies that immunoselectively bind to GPCRX polypeptides, or fragments, homologs, analogs or derivatives thereof.

5 In another aspect, the invention includes pharmaceutical compositions that include therapeutically- or prophylactically-effective amounts of a therapeutic and a pharmaceutically-acceptable carrier. The therapeutic can be, e.g., a GPCRX nucleic acid, a GPCRX polypeptide, or an antibody specific for a GPCRX polypeptide. In a further aspect, the invention includes, in one or more containers, a therapeutically- or prophylactically-

10 effective amount of this pharmaceutical composition.

In a further aspect, the invention includes a method of producing a polypeptide by culturing a cell that includes a GPCRX nucleic acid, under conditions allowing for expression of the GPCRX polypeptide encoded by the DNA. If desired, the GPCRX polypeptide can then be recovered.

15 In another aspect, the invention includes a method of detecting the presence of a GPCRX polypeptide in a sample. In the method, a sample is contacted with a compound that selectively binds to the polypeptide under conditions allowing for formation of a complex between the polypeptide and the compound. The complex is detected, if present, thereby identifying the GPCRX polypeptide within the sample.

20 The invention also includes methods to identify specific cell or tissue types based on their expression of a GPCRX.

Also included in the invention is a method of detecting the presence of a GPCRX nucleic acid molecule in a sample by contacting the sample with a GPCRX nucleic acid probe or primer, and detecting whether the nucleic acid probe or primer bound to a GPCRX

25 nucleic acid molecule in the sample.

In a further aspect, the invention provides a method for modulating the activity of a GPCRX polypeptide by contacting a cell sample that includes the GPCRX polypeptide with a compound that binds to the GPCRX polypeptide in an amount sufficient to modulate the activity of said polypeptide. The compound can be, e.g., a small molecule, such as a nucleic

30 acid, peptide, polypeptide, peptidomimetic, carbohydrate, lipid or other organic (carbon containing) or inorganic molecule, as further described herein.

Also within the scope of the invention is the use of a therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, e.g.,

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developmental diseases; MHCII and III diseases (immune diseases); taste and scent detectability disorders; Burkitt's lymphoma; corticoneurogenic disease; signal transduction pathway disorders; metabolic pathway disorders; retinal diseases including those involving photoreception; cell growth rate disorders; cell shape disorders; metabolic disorders; feeding

5   disorders; control of feeding; the metabolic syndrome X; wasting disorders associated with chronic diseases; obesity; potential obesity due to over-eating or metabolic disturbances; potential disorders due to starvation (lack of appetite); diabetes; noninsulin-dependent diabetes mellitus (NIDDM1); infectious disease; bacterial, fungal, protozoal and viral infections (particularly infections caused by HIV-1 or HIV-2); pain; cancer (including but not

10   limited to neoplasm; adenocarcinoma; lymphoma; prostate cancer; uterus cancer); cancer-associated cachexia; anorexia; bulimia; asthma; Parkinson's disease; acute heart failure; hypotension; hypertension; urinary retention; osteoporosis; Crohn's disease; multiple sclerosis; Albright Hereditary Ostoeodystrophy; angina pectoris; myocardial infarction; ulcers; allergies; benign prostatic hypertrophy; and psychotic and neurological disorders;

15   including anxiety; schizophrenia; manic depression; delirium; dementia; neurodegenerative disorders; Alzheimer's disease; severe mental retardation; Dentatorubro-pallidoluysian atrophy (DRPLA); Hypophosphatemic rickets; autosomal dominant (2) acrocallosal syndrome and dyskinesias, such as Huntington's disease or Gilles de la Tourette syndrome; immune disorders; adrenoleukodystrophy; congenital adrenal hyperplasia; hemophilia;

20   hypercoagulation; idiopathic thrombocytopenic purpura; autoimmume disease; immunodeficiencies; transplantation; Von Hippel-Lindau (VHL) syndrome; stroke; tuberous sclerosis; hypercalceimia; cerebral palsy; epilepsy; Lesch-Nyhan syndrome; ataxia-telangiectasia; Leukodystrophies; Behavioral disorders; Addiction; Neuroprotection; cirrhosis; transplantation; systemic lupus erythematosus; emphysema; scleroderma; ARDS;

25   renal artery stenosis; interstitial nephritis; glomerulonephritis; polycystic kidney disease; systemic lupus erythematosus; renal tubular acidosis; IgA nephropathy; cardiomyopathy; atherosclerosis; congenital heart defects; aortic stenosis ; atrial septal defect (ASD); atrioventricular (A-V) canal defect; ductus arteriosus; pulmonary stenosis ; subaortic stenosis; ventricular septal defect (VSD); valve diseases; scleroderma; fertility; pancreatitis; endocrine

30   dysfunctions; growth and reproductive disorders; inflammatory bowel disease; diverticular disease; leukodystrophies; graft vesus host; hyperthyroidism; endometriosis; hematopoietic disorders and/or other pathologies and disorders of the like. The therapeutic can be, *e.g.*, a

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GPCRX nucleic acid, a GPCRX polypeptide, or a GPCRX-specific antibody, or biologically-active derivatives or fragments thereof.

For example, the compositions of the present invention will have efficacy for treatment of patients suffering from the diseases and disorders listed above and/or other pathologies and disorders.

The polypeptides can be used as immunogens to produce antibodies specific for the invention, and as vaccines. They can also be used to screen for potential agonist and antagonist compounds. For example, a cDNA encoding GPCRX may be useful in gene therapy, and GPCRX may be useful when administered to a subject in need thereof. By way of nonlimiting example, the compositions of the present invention will have efficacy for treatment of patients suffering the diseases and disorders listed above and/or other pathologies and disorders.

The invention further includes a method for screening for a modulator of disorders or syndromes including, *e.g.*, diseases and disorders listed above and/or other pathologies and disorders and those disorders related to cell signal processing and metabolic pathway modulation. The method includes contacting a test compound with a GPCRX polypeptide and determining if the test compound binds to said GPCRX polypeptide. Binding of the test compound to the GPCRX polypeptide indicates the test compound is a modulator of activity, or of latency or predisposition to the aforementioned disorders or syndromes.

Also within the scope of the invention is a method for screening for a modulator of activity, or of latency or predisposition to an disorders or syndromes including the diseases and disorders listed above and/or other pathologies and disorders or other disorders related to cell signal processing and metabolic pathway modulation by administering a test compound to a test animal at increased risk for the aforementioned disorders or syndromes. The test animal expresses a recombinant polypeptide encoded by a GPCRX nucleic acid. Expression or activity of GPCRX polypeptide is then measured in the test animal, as is expression or activity of the protein in a control animal which recombinantly-expresses GPCRX polypeptide and is not at increased risk for the disorder or syndrome. Next, the expression of GPCRX polypeptide in both the test animal and the control animal is compared. A change in the activity of GPCRX polypeptide in the test animal relative to the control animal indicates the test compound is a modulator of latency of the disorder or syndrome.

In yet another aspect, the invention includes a method for determining the presence of or predisposition to a disease associated with altered levels of a GPCRX polypeptide, a

GPCRX nucleic acid, or both, in a subject (*e.g.*, a human subject). The method includes measuring the amount of the GPCRX polypeptide in a test sample from the subject and comparing the amount of the polypeptide in the test sample to the amount of the GPCRX polypeptide present in a control sample. An alteration in the level of the GPCRX polypeptide

5   in the test sample as compared to the control sample indicates the presence of or predisposition to a disease in the subject. Preferably, the predisposition includes diseases and disorders listed above and/or other pathologies and disorders. Also, the expression levels of the new polypeptides of the invention can be used in a method to screen for various cancers as well as to determine the stage of cancers.

10   In a further aspect, the invention includes a method of treating or preventing a pathological condition associated with a disorder in a mammal by administering to the subject a GPCRX polypeptide, a GPCRX nucleic acid, or a GPCRX-specific antibody to a subject (*e.g.*, a human subject), in an amount sufficient to alleviate or prevent the pathological condition. In preferred embodiments, the disorder, includes the diseases and disorders listed

15   above and/or other pathologies and disorders.

In yet another aspect, the invention can be used in a method to identity the cellular receptors and downstream effectors of the invention by any one of a number of techniques commonly employed in the art. These include but are not limited to the two-hybrid system, affinity purification, co-precipitation with antibodies or other specific-interacting molecules.

20   Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references

25   mentioned herein are incorporated by reference in their entirety. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

DETAILED DESCRIPTION OF THE INVENTION

The invention is based, in part, upon the discovery of novel nucleic acid sequences that encode novel polypeptides. The nucleic acids, and their encoded polypeptides, are collectively designated herein as "GPCRX".

5   The novel GPCRX nucleic acids of the invention include the nucleic acids whose sequences are provided in Table 1 (at the end of the Detailed Description), or a fragment, derivative, analog or homolog thereof. The individual GPCRX nucleic acids and proteins are described below. All of the sequences listed in the attached Table 1 have a high degree of homology to known GPCR sequences. Exemplary homology for the sequences

10   is provided in the provisional applications from which the present application claims priority. This homology data are incorporated herein by reference in their entirety. Within the scope of this invention is a method of using these nucleic acids and peptides in the treatment or prevention of a disorder related to cell signaling or metabolic pathway modulation.

G-Protein Coupled Receptor proteins ("GPCRs") have been identified as a large

15   family of G protein-coupled receptors in a number of species. These receptors share a seven transmembrane domain structure with many neurotransmitter and hormone receptors, and are likely to underlie the recognition and G-protein-mediated transduction of various signals. Human GPCR generally do not contain introns and belong to four different gene subfamilies, displaying great sequence variability. These genes are dominantly expressed in olfactory

20   epithelium. See, e.g., Ben-Arie et al., *Hum. Mol. Genet.* 1994 3:229-235; and, Online Mendelian Inheritance in Man ("OMIM") entry#164342(http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?).

The olfactory receptor ("OR") gene family constitutes one of the largest GPCR multigene families and is distributed among many chromosomal sites in the human genome.

25   See Rouquier et al., *Hum. Mol. Genet.* 7(9):1337-45 (1998); Malnic et al., *Cell* 96:713-23 (1999). Olfactory receptors constitute the largest family among G protein-coupled receptors, with up to 1000 members expected. See Vanderhaeghen et al., *Genomics* 39(3):239-46 (1997); Xie et al., *Mamm. Genome* 11(12):1070-78 (2000); Issel-Tarver et al., *Proc. Natl. Acad. Sci. USA* 93(20):10897-902 (1996). The recognition of odorants by olfactory receptors

30   is the first stage in odor discrimination. See Krautwurst et al., *Cell* 95(7):917-26 (1998); Buck et al., *Cell* 65(1):175-87 (1991). Many ORs share some characteristic sequence motifs

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and have a central variable region corresponding to a putative ligand binding site. See Issel-Tarver et al., *Proc. Natl. Acad. Sci. USA* 93:10897-902 (1996).

Other examples of seven membrane spanning proteins that are related to GPCRs are chemoreceptors. See Thomas et al., Gene 178(1-2):1-5 (1996). Chemoreceptors have been identified in taste, olfactory, and male reproductive tissues. See *id*.; Walensky et al., *J. Biol. Chem.* 273(16):9378-87 (1998); Parmentier et al., *Nature* 355(6359):453-55 (1992); Asai et al., *Biochem. Biophys. Res. Commun.* 221(2):240-47 (1996).

The GPCRX nucleic acids of the invention encoding GPCR-like proteins include the nucleic acids whose sequences are provided herein, or fragments thereof. The invention also includes mutant or variant nucleic acids any of whose bases may be changed from the corresponding base shown herein while still encoding a protein that maintains its GPCR-like activities and physiological functions, or a fragment of such a nucleic acid. The invention further includes nucleic acids whose sequences are complementary to those just described, including nucleic acid fragments that are complementary to any of the nucleic acids just described. The invention additionally includes nucleic acids or nucleic acid fragments, or complements thereto, whose structures include chemical modifications. Such modifications include, by way of nonlimiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be used, for example, as antisense binding nucleic acids in therapeutic applications in a subject.

The GPCRX proteins of the invention include the GPCR-like proteins whose sequences are provided herein. The invention also includes mutant or variant proteins any of whose residues may be changed from the corresponding residue shown herein while still encoding a protein that maintains its GPCR-like activities and physiological functions, or a functional fragment thereof. The invention further encompasses antibodies and antibody fragments, such as F_{ab} or $(F_{ab})_2$, that bind immunospecifically to any of the proteins of the invention.

The GPCRX nucleic acids and proteins are useful in potential therapeutic applications implicated in various GPCR-related pathological disorders and/or OR-related pathological disorders, described further below. For example, a cDNA encoding the GPCR (or olfactory-receptor) like protein may be useful in gene therapy, and the receptor -like protein may be useful when administered to a subject in need thereof. The nucleic acids and proteins of the invention are also useful in potential therapeutic applications used in the treatment of

developmental diseases; MHCII and III diseases (immune diseases); taste and scent detectability disorders; Burkitt's lymphoma; corticoneurogenic disease; signal transduction pathway disorders; metabolic pathway disorders; retinal diseases including those involving photoreception; cell growth rate disorders; cell shape disorders; metabolic disorders; feeding disorders; control of feeding; the metabolic syndrome X; wasting disorders associated with chronic diseases; obesity; potential obesity due to over-eating or metabolic disturbances; potential disorders due to starvation (lack of appetite); diabetes; noninsulin-dependent diabetes mellitus (NIDDM1); infectious disease; bacterial, fungal, protozoal and viral infections (particularly infections caused by HIV-1 or HIV-2); pain; cancer (including but not limited to neoplasm; adenocarcinoma; lymphoma; prostate cancer; uterus cancer); cancer-associated cachexia; anorexia; bulimia; asthma; Parkinson's disease; acute heart failure; hypotension; hypertension; urinary retention; osteoporosis; Crohn's disease; multiple sclerosis; Albright hereditary ostoeodystrophy; angina pectoris; myocardial infarction; ulcers; allergies; benign prostatic hypertrophy; and psychotic and neurological disorders; including anxiety; schizophrenia; manic depression; delirium; dementia; neurodegenerative disorders; Alzheimer's disease; severe mental retardation; dentatorubro-pallidoluysian atrophy (DRPLA); hypophosphatemic rickets; autosomal dominant (2) acrocallosal syndrome and dyskinesias, such as Huntington's disease or Gilles de la Tourette syndrome; immune disorders; adrenoleukodystrophy; congenital adrenal hyperplasia; hemophilia; hypercoagulation; idiopathic thrombocytopenic purpura; autoimmume disease; immunodeficiencies; transplantation; Von Hippel-Lindau (VHL) syndrome; stroke; tuberous sclerosis; hypercalceimia; cerebral palsy; epilepsy; Lesch-Nyhan syndrome; ataxia-telangiectasia; leukodystrophies; behavioral disorders; addiction; neuroprotection; cirrhosis; transplantation; systemic lupus erythematosus; emphysema; scleroderma; ARDS; renal artery stenosis; interstitial nephritis; glomerulonephritis; polycystic kidney disease; systemic lupus erythematosus; renal tubular acidosis; IgA nephropathy; cardiomyopathy; atherosclerosis; congenital heart defects; aortic stenosis ; atrial septal defect (ASD); atrioventricular (A-V) canal defect; ductus arteriosus; pulmonary stenosis ; subaortic stenosis; ventricular septal defect (VSD); valve diseases; scleroderma; fertility; pancreatitis; endocrine dysfunctions; growth and reproductive disorders; inflammatory bowel disease; diverticular disease; leukodystrophies; graft vesus host; hyperthyroidism; endometriosis; hematopoietic disorders and/or other pathologies and disorders. Other GPCR-related diseases and disorders are contemplated.

The protein similarity information, expression pattern, and map location for the olfactory receptor-like GPCR proteins and nucleic acids disclosed herein suggest that these olfactory receptors may have important structural and/or physiological functions characteristic of the olfactory receptor family. Therefore, the GPCR nucleic acids and

5   proteins are useful in potential diagnostic and therapeutic applications and as a research tool. These include serving as a specific or selective nucleic acid or protein diagnostic and/or prognostic marker, wherein the presence or amount of the nucleic acid or the protein are to be assessed, as well as potential therapeutic applications such as the following: (i) a protein therapeutic, (ii) a small molecule drug target, (iii) an antibody target (therapeutic, diagnostic,

10   drug targeting/cytotoxic antibody), (iv) a nucleic acid useful in gene therapy (gene delivery/gene ablation), and (v) a composition promoting tissue regeneration in vitro and in vivo (vi) biological defense weapon.

GPCR polypeptides are useful in the generation of antibodies that bind immunospecifically to the GPCR polypeptides of the invention, and as vaccines. The

15   antibodies are for use in therapeutic or diagnostic methods. These antibodies may be generated according to methods known in the art, using prediction from hydrophobicity charts, as described in the "Anti-GPCRX Antibodies" section below.

GPCR polypeptides can also be used to screen for potential agonist and antagonist compounds. For example, a cDNA encoding the GPCR-like protein may be useful in gene

20   therapy, and the GPCR-like protein may be useful when administered to a subject in need thereof. By way of nonlimiting example, the compositions of the present invention will have efficacy for treatment of patients suffering from the diseases and disorders disclosed above and/or other pathologies and disorders. The novel nucleic acid encoding GPCR-like protein, and the GPCR-like protein of the invention, or fragments thereof, may further be useful in

25   diagnostic applications, wherein the presence or amount of the nucleic acid or the protein are to be assessed.

GPCRX Nucleic Acids and Polypeptides

One aspect of the invention pertains to isolated nucleic acid molecules that encode GPCRX polypeptides or biologically active portions thereof. Also included in the invention

30   are nucleic acid fragments sufficient for use as hybridization probes to identify GPCRX-encoding nucleic acids (e.g., GPCRX mRNAs) and fragments for use as PCR primers for the amplification and/or mutation of GPCRX nucleic acid molecules. As used herein, the term

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"nucleic acid molecule" is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA), RNA molecules (*e.g.*, mRNA), analogs of the DNA or RNA generated using nucleotide analogs, and derivatives, fragments and homologs thereof. The nucleic acid molecule may be single-stranded or double-stranded, but preferably is comprised double-stranded DNA.

A GPCRX nucleic acid can encode a mature GPCRX polypeptide. As used herein, a "mature" form of a polypeptide or protein disclosed in the present invention is the product of a naturally occurring polypeptide or precursor form or proprotein. The naturally occurring polypeptide, precursor or proprotein includes, by way of nonlimiting example, the full-length gene product, encoded by the corresponding gene. Alternatively, it may be defined as the polypeptide, precursor or proprotein encoded by an ORF described herein. The product "mature" form arises, again by way of nonlimiting example, as a result of one or more naturally occurring processing steps as they may take place within the cell, or host cell, in which the gene product arises. Examples of such processing steps leading to a "mature" form of a polypeptide or protein include the cleavage of the N-terminal methionine residue encoded by the initiation codon of an ORF, or the proteolytic cleavage of a signal peptide or leader sequence. Thus a mature form arising from a precursor polypeptide or protein that has residues 1 to N, where residue 1 is the N-terminal methionine, would have residues 2 through N remaining after removal of the N-terminal methionine. Alternatively, a mature form arising from a precursor polypeptide or protein having residues 1 to N, in which an N-terminal signal sequence from residue 1 to residue M is cleaved, would have the residues from residue M+1 to residue N remaining. Further as used herein, a "mature" form of a polypeptide or protein may arise from a step of post-translational modification other than a proteolytic cleavage event. Such additional processes include, by way of non-limiting example, glycosylation, myristoylation or phosphorylation. In general, a mature polypeptide or protein may result from the operation of only one of these processes, or a combination of any of them.

The term "probes", as utilized herein, refers to nucleic acid sequences of variable length, preferably between at least about 10 nucleotides (nt), 100 nt, or as many as approximately, *e.g.*, 6,000 nt, depending upon the specific use. Probes are used in the detection of identical, similar, or complementary nucleic acid sequences. Longer length probes are generally obtained from a natural or recombinant source, are highly specific, and much slower to hybridize than shorter-length oligomer probes. Probes may be single- or

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double-stranded and designed to have specificity in PCR, membrane-based hybridization technologies, or ELISA-like technologies.

The term "isolated" nucleic acid molecule, as utilized herein, is one, which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5'- and 3'-termini of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated GPCRX nucleic acid molecules can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell/tissue from which the nucleic acid is derived (*e.g.*, brain, heart, liver, spleen, etc.). Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material or culture medium when produced by recombinant techniques, or of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 or a complement of this aforementioned nucleotide sequence, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 as a hybridization probe, GPCRX molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, *et al.*, (eds.), MOLECULAR CLONING: A LABORATORY MANUAL 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989; and Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993.)

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A nucleic acid of the invention can be amplified using cDNA, mRNA or alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore,

5   oligonucleotides corresponding to GPCRX nucleotide sequences can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

As used herein, the term "oligonucleotide" refers to a series of linked nucleotide residues, which oligonucleotide has a sufficient number of nucleotide bases to be used in a PCR reaction. A short oligonucleotide sequence may be based on, or designed from, a

10   genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an identical, similar or complementary DNA or RNA in a particular cell or tissue. Oligonucleotides comprise portions of a nucleic acid sequence having about 10 nt, 50 nt, or 100 nt in length, preferably about 15 nt to 30 nt in length. In one embodiment of the invention, an oligonucleotide comprising a nucleic acid molecule less than 100 nt in length

15   would further comprise at least 6 contiguous nucleotides of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181,

20   183, 185, 187, 189, 191, 193, 195, 197 and 199, or a complement thereof. Oligonucleotides may be chemically synthesized and may also be used as probes.

In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule that is a complement of the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49,

25   51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199, or a portion of this nucleotide sequence (e.g., a fragment that can be used as a probe or primer or a fragment

30   encoding a biologically-active portion of a GPCRX polypeptide). A nucleic acid molecule that is complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109,

13

111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 is one that is sufficiently complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25,

5   27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 that it can hydrogen bond with little or no mismatches to the

10   nucleotide sequence shown SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193,

15   195, 197 and 199, thereby forming a stable duplex.

As used herein, the term "complementary" refers to Watson-Crick or Hoogsteen base pairing between nucleotides units of a nucleic acid molecule, and the term "binding" means the physical or chemical interaction between two polypeptides or compounds or associated polypeptides or compounds or combinations thereof. Binding includes ionic, non-ionic, van

20   der Waals, hydrophobic interactions, and the like. A physical interaction can be either direct or indirect. Indirect interactions may be through or due to the effects of another polypeptide or compound. Direct binding refers to interactions that do not take place through, or due to, the effect of another polypeptide or compound, but instead are without other substantial chemical intermediates.

25   Fragments provided herein are defined as sequences of at least 6 (contiguous) nucleic acids or at least 4 (contiguous) amino acids, a length sufficient to allow for specific hybridization in the case of nucleic acids or for specific recognition of an epitope in the case of amino acids, respectively, and are at most some portion less than a full length sequence. Fragments may be derived from any contiguous portion of a nucleic acid or amino acid

30   sequence of choice. Derivatives are nucleic acid sequences or amino acid sequences formed from the native compounds either directly or by modification or partial substitution. Analogs are nucleic acid sequences or amino acid sequences that have a structure similar to, but not identical to, the native compound but differs from it in respect to certain components or side

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chains. Analogs may be synthetic or from a different evolutionary origin and may have a similar or opposite metabolic activity compared to wild type. Homologs are nucleic acid sequences or amino acid sequences of a particular gene that are derived from different species.

5   Derivatives and analogs may be full length or other than full length, if the derivative or analog contains a modified nucleic acid or amino acid, as described below. Derivatives or analogs of the nucleic acids or proteins of the invention include, but are not limited to, molecules comprising regions that are substantially homologous to the nucleic acids or proteins of the invention, in various embodiments, by at least about 70%, 80%, or 95%

10   identity (with a preferred identity of 80-95%) over a nucleic acid or amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to the complement of a sequence encoding the aforementioned proteins under stringent, moderately stringent, or low stringent conditions. See *e.g.* Ausubel, *et al.*,

15   CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993, and below.

           A "homologous nucleic acid sequence" or "homologous amino acid sequence," or variations thereof, refer to sequences characterized by a homology at the nucleotide level or amino acid level as discussed above. Homologous nucleotide sequences encode those

20   sequences coding for isoforms of GPCRX polypeptides. Isoforms can be expressed in different tissues of the same organism as a result of, for example, alternative splicing of RNA. Alternatively, isoforms can be encoded by different genes. In the invention, homologous nucleotide sequences include nucleotide sequences encoding for a GPCRX polypeptide of species other than humans, including, but not limited to: vertebrates, and thus

25   can include, *e.g.*, frog, mouse, rat, rabbit, dog, cat cow, horse, and other organisms. Homologous nucleotide sequences also include, but are not limited to, naturally occurring allelic variations and mutations of the nucleotide sequences set forth herein. A homologous nucleotide sequence does not, however, include the exact nucleotide sequence encoding huma GPCRX protein. Homologous nucleic acid sequences include those nucleic acid

30   sequences that encode conservative amino acid substitutions (see below) in SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137,

139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199, as well as a polypeptide possessing GPCRX biological activity. Various biological activities of the GPCRX proteins are described below.

5　　　　A GPCRX polypeptide is encoded by the open reading frame ("ORF") of a GPCRX nucleic acid. An ORF corresponds to a nucleotide sequence that could potentially be translated into a polypeptide. A stretch of nucleic acids comprising an ORF is uninterrupted by a stop codon. An ORF that represents the coding sequence for a full protein begins with an ATG "start" codon and terminates with one of the three "stop" codons, namely, TAA, 10　　TAG, or TGA. For the purposes of this invention, an ORF may be any part of a coding sequence, with or without a start codon, a stop codon, or both. For an ORF to be considered as a good candidate for coding for a *bona fide* cellular protein, a minimum size requirement is often set, *e.g.,* a stretch of DNA that would encode a protein of 50 amino acids or more.

　　　　The nucleotide sequences determined from the cloning of the huma GPCRX genes 15　　allows for the generation of probes and primers designed for use in identifying and/or cloning GPCRX homologues in other cell types, *e.g.* from other tissues, as well as GPCRX homologues from other vertebrates. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, 25, 50, 100, 150, 200, 20　　250, 300, 350 or 400 consecutive sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 25　　179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199; or an anti-sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 30　　165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199; or of a naturally occurring mutant of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117,

119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199.

Probes based on the huma GPCRX nucleotide sequences can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. In various embodiments, the probe further comprises a label group attached thereto, *e.g.* the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express a GPCRX protein, such as by measuring a level of a GPCRX-encoding nucleic acid in a sample of cells from a subject *e.g.*, detecting GPCRX mRNA levels or determining whether a genomic GPCRX gene has been mutated or deleted.

"A polypeptide having a biologically-active portion of a GPCRX polypeptide" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. A nucleic acid fragment encoding a "biologically-active portion of GPCRX" can be prepared by isolating a portion SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 that encodes a polypeptide having a GPCRX biological activity (the biological activities of the GPCRX proteins are described below), expressing the encoded portion of GPCRX protein (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of GPCRX.

GPCRX Nucleic Acid and Polypeptide Variants

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequences shown SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 due to degeneracy of the genetic code and thus encode the same GPCRX

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proteins as that encoded by the nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 11,

13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61,

63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107,

109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143,

5   145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179,

181, 183, 185, 187, 189, 191, 193, 195, 197 and 199. In another embodiment, an isolated

nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having

an amino acid sequence shown in SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26,

28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76,

10   78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118,

120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154,

156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190,

192, 194, 196, 198 and 200. In addition to the huma GPCRX nucleotide sequences shown in

SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45,

15   47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95,

97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133,

135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169,

171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 it will be

appreciated by those skilled in the art that DNA sequence polymorphisms that lead to

20   changes in the amino acid sequences of the GPCRX polypeptides may exist within a

population (e.g., the human population). Such genetic polymorphism in the GPCRX genes

may exist among individuals within a population due to natural allelic variation. As used

herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising

an open reading frame (ORF) encoding a GPCRX protein, preferably a vertebrate GPCRX

25   protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide

sequence of the GPCRX genes. Any and all such nucleotide variations and resulting amino

acid polymorphisms in the GPCRX polypeptides, which are the result of natural allelic

variation and that do not alter the functional activity of the GPCRX polypeptides, are

intended to be within the scope of the invention.

30   Moreover, nucleic acid molecules encoding GPCRX proteins from other species, and

thus that have a nucleotide sequence that differs from the human sequence SEQ ID NOS:1, 3,

5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55,

57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103,

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105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and

5   homologues of the GPCRX cDNAs of the invention can be isolated based on their homology to the huma GPCRX nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

Accordingly, in another embodiment, an isolated nucleic acid molecule of the
10   invention is at least 6 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143,
15   145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199. In another embodiment, the nucleic acid is at least 10, 25, 50, 100, 250, 500, 750, 1000, 1500, or 2000 or more nucleotides in length. In yet another embodiment, an isolated nucleic acid molecule of the invention hybridizes to the coding region. As used herein, the term "hybridizes under stringent
20   conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other.

Homologs (i.e., nucleic acids encoding GPCRX proteins derived from species other than human) or other related sequences (e.g., paralogs) can be obtained by low, moderate or
25   high stringency hybridization with all or a portion of the particular human sequence as a probe using methods well known in the art for nucleic acid hybridization and cloning.

As used herein, the phrase "stringent hybridization conditions" refers to conditions under which a probe, primer or oligonucleotide will hybridize to its target sequence, but to no other sequences. Stringent conditions are sequence-dependent and will be different in
30   different circumstances. Longer sequences hybridize specifically at higher temperatures than shorter sequences. Generally, stringent conditions are selected to be about 5 °C lower than the thermal melting point (Tm) for the specific sequence at a defined ionic strength and pH. The Tm is the temperature (under defined ionic strength, pH and nucleic acid concentration) at

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which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. Since the target sequences are generally present at excess, at Tm, 50% of the probes are occupied at equilibrium. Typically, stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to

5   1.0 M sodium ion (or other salts) at

pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes, primers or oligonucleotides (e.g., 10 nt to 50 nt) and at least about 60°C for longer probes, primers and oligonucleotides. Stringent conditions may also be achieved with the addition of destabilizing agents, such as formamide.

10   Stringent conditions are known to those skilled in the art and can be found in Ausubel, et al., (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. Preferably, the conditions are such that sequences at least about 65%, 70%, 75%, 85%, 90%, 95%, 98%, or 99% homologous to each other typically remain hybridized to each other. A non-limiting example of stringent hybridization conditions are

15   hybridization in a high salt buffer comprising 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 mg/ml denatured salmon sperm DNA at 65°C, followed by one or more washes in 0.2X SSC, 0.01% BSA at 50°C. An isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequences of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35,

20   37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 corresponds to a naturally-occurring nucleic acid molecule. As used herein, a

25   "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

       In a second embodiment, a nucleic acid sequence that is hybridizable to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65,

30   67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 or fragments, analogs or derivatives thereof, under

conditions of moderate stringency is provided. A non-limiting example of moderate stringency hybridization conditions are hybridization in 6X SSC, 5X Denhardt's solution, 0.5% SDS and 100 mg/ml denatured salmon sperm DNA at 55°C, followed by one or more washes in 1X SSC, 0.1% SDS at 37°C. Other conditions of moderate stringency that may be

5   used are well-known within the art. See, *e.g.*, Ausubel, et *al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990; GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY.

In a third embodiment, a nucleic acid that is hybridizable to the nucleic acid molecule comprising the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23,

10   25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 or fragments, analogs or derivatives thereof, under conditions of

15   low stringency, is provided. A non-limiting example of low stringency hybridization conditions are hybridization in 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 mg/ml denatured salmon sperm DNA, 10% (wt/vol) dextran sulfate at 40°C, followed by one or more washes in 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS at 50°C. Other conditions of low stringency

20   that may be used are well known in the art (*e.g.*, as employed for cross-species hybridizations). See, *e.g.*, Ausubel, *et al.* (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990, GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY; Shilo and Weinberg, 1981. *Proc Natl Acad Sci USA* **78**: 6789-6792.

25

Conservative Mutations

In addition to naturally-occurring allelic variants of GPCRX sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21,

30   23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187,

189, 191, 193, 195, 197 and 199 thereby leading to changes in the amino acid sequences of the encoded GPCRX proteins, without altering the functional ability of said GPCRX proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16,

5   18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200. A "non-essential" amino acid residue is a

10   residue that can be altered from the wild-type sequences of the GPCRX proteins without altering their biological activity, whereas an "essential" amino acid residue is required for such biological activity. For example, amino acid residues that are conserved among the GPCRX proteins of the invention are predicted to be particularly non-amenable to alteration. Amino acids for which conservative substitutions can be made are well-known within the art.

15   Another aspect of the invention pertains to nucleic acid molecules encoding GPCRX proteins that contain changes in amino acid residues that are not essential for activity. Such GPCRX proteins differ in amino acid sequence from SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110,

20   112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200 yet retain biological activity. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 45%

25   homologous to the amino acid sequences of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186,

30   188, 190, 192, 194, 196, 198 and 200. Preferably, the protein encoded by the nucleic acid molecule is at least about 60% homologous to SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114,

22

116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200; more preferably at least about 70% homologous to SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44,

5   46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200; still more preferably at least about 80% homologous to SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20,

10 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200; even more preferably at least about 90% homologous

15 to SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200; and

20 most preferably at least about 95% homologous to SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184,

25 186, 188, 190, 192, 194, 196, 198 and 200. An isolated nucleic acid molecule encoding a GPCRX protein homologous to the protein of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150,

30 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59,

61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105,
107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141,
143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177,
179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 such that one or more amino acid

5   substitutions, additions or deletions are introduced into the encoded protein.

Mutations can be introduced into SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22,
24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72,
74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116,
118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152,

10   154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188,
190, 192, 194, 196, 198 and 200 by standard techniques, such as site-directed mutagenesis
and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made
at one or more predicted, non-essential amino acid residues. A "conservative amino acid
substitution" is one in which the amino acid residue is replaced with an amino acid residue

15   having a similar side chain. Families of amino acid residues having similar side chains have
been defined within the art. These families include amino acids with basic side chains (e.g.,
lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged
polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine),
nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine,

20   methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and
aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted
non-essential amino acid residue in the GPCRX protein is replaced with another amino acid
residue from the same side chain family. Alternatively, in another embodiment, mutations
can be introduced randomly along all or part of a GPCRX coding sequence, such as by

25   saturation mutagenesis, and the resultant mutants can be screened for GPCRX biological
activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NOS:1, 3,
5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55,
57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103,
105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139,

30   141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175,
177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199, the encoded protein can be
expressed by any recombinant technology known in the art and the activity of the protein can
be determined.

The relatedness of amino acid families may also be determined based on side chain interactions. Substituted amino acids may be fully conserved "strong" residues or fully conserved "weak" residues. The "strong" group of conserved amino acid residues may be any one of the following groups: STA, NEQK, NHQK, NDEQ, QHRK, MILV, MILF, HY,

5 FYW, wherein the single letter amino acid codes are grouped by those amino acids that may be substituted for each other. Likewise, the "weak" group of conserved residues may be any one of the following: CSA, ATV, SAG, STNK, STPA, SGND, SNDEQK, NDEQHK, NEQHRK, VLIM, HFY, wherein the letters within each group represent the single letter amino acid code.

10 In one embodiment, a mutant GPCRX protein can be assayed for (*i*) the ability to form protein:protein interactions with other GPCRX proteins, other cell-surface proteins, or biologically-active portions thereof, (*ii*) complex formation between a mutant GPCRX protein and a GPCRX ligand; or (*iii*) the ability of a mutant GPCRX protein to bind to an intracellular target protein or biologically-active portion thereof; (*e.g.* avidin proteins).

15 In yet another embodiment, a mutant GPCRX protein can be assayed for the ability to regulate a specific biological function (*e.g.*, regulation of insulin release).

Antisense Nucleic Acids

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the

20 nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197

25 and 199, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein (*e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence). In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250

30 or 500 nucleotides or an entire GPCRX coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of a GPCRX protein of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43,

45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199, or

5   antisense nucleic acids complementary to a GPCRX nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171,

10   173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199, are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding a GPCRX protein. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are

15   translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding the GPCRX protein. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (i.e., also referred to as 5' and 3' untranslated regions).

20   Given the coding strand sequences encoding the GPCRX protein disclosed herein, antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of GPCRX mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of GPCRX mRNA. For

25   example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of GPCRX mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense

30   oligonucleotide) can be chemically synthesized using naturally-occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense

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nucleic acids (e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used).

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated in situ such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a GPCRX protein to thereby inhibit expression of the protein (e.g., by inhibiting transcription and/or translation). The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface (e.g., by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens). The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve

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sufficient nucleic acid molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other. See, e.g., Gaultier, et al., 1987. Nucl. Acids Res. **15**: 6625-6641. The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (see, e.g., Inoue, et al. 1987. Nucl. Acids Res. **15**: 6131-6148) or a chimeric RNA-DNA analogue (see, e.g., Inoue, et al., 1987. FEBS Lett. **215**: 327-330.

Ribozymes and PNA Moieties

Nucleic acid modifications include, by way of non-limiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be used, for example, as antisense binding nucleic acids in therapeutic applications in a subject.

In one embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes as described in Haselhoff and Gerlach 1988. Nature 334: 585-591) can be used to catalytically cleave GPCRX mRNA transcripts to thereby inhibit translation of GPCRX mRNA. A ribozyme having specificity for a GPCRX-encoding nucleic acid can be designed based upon the nucleotide sequence of a GPCRX cDNA disclosed herein (i.e., SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a GPCRX-encoding mRNA. See, e.g., U.S. Patent 4,987,071 to Cech, et al. and U.S. Patent 5,116,742 to Cech, et al. GPCRX mRNA can also be used to select a catalytic RNA having a specific ribonuclease

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activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, GPCRX gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the GPCRX nucleic acid (*e.g.*, the

5   GPCRX promoter and/or enhancers) to form triple helical structures that prevent transcription of the GPCRX gene in target cells. *See, e.g.*, Helene, 1991. *Anticancer Drug Des.* 6: 569-84; Helene, *et al.* 1992. *Ann. N.Y. Acad. Sci.* 660: 27-36; Maher, 1992. *Bioassays* 14: 807-15.

In various embodiments, the GPCRX nucleic acids can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or

10   solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids. *See, e.g.*, Hyrup, *et al.*, 1996. *Bioorg Med Chem* 4: 5-23. As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics (*e.g.*, DNA mimics) in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained.

15   The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup, *et al.*, 1996. *supra*; Perry-O'Keefe, *et al.*, 1996. *Proc. Natl. Acad. Sci. USA* 93: 14670-14675.

PNAs of GPCRX can be used in therapeutic and diagnostic applications. For

20   example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs of GPCRX can also be used, for example, in the analysis of single base pair mutations in a gene (*e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S_1 nucleases (*see*, Hyrup, *et al.*,

25   1996.*supra*); or as probes or primers for DNA sequence and hybridization (*see*, Hyrup, *et al.*, 1996, *supra*; Perry-O'Keefe, *et al.*, 1996. *supra*).

In another embodiment, PNAs of GPCRX can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug

30   delivery known in the art. For example, PNA-DNA chimeras of GPCRX can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes (*e.g.*, RNase H and DNA polymerases) to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA

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chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (*see*, Hyrup, et al., 1996. *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup, *et al.*, 1996. *supra* and Finn, *et al.*, 1996. *Nucl Acids Res* 24: 3357-3363. For example, a DNA chain can

5 be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA. *See, e.g.*, Mag, *et al.*, 1989. *Nucl Acid Res* 17: 5973-5988. PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment. *See,*

10 *e.g.*, Finn, *et al.*, 1996. *supra*. Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. *See, e.g.*, Petersen, *et al.*, 1975. *Bioorg. Med. Chem. Lett.* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport

15 across the cell membrane (*see, e.g.*, Letsinger, *et al.*, 1989. *Proc. Natl. Acad. Sci. U.S.A.* 86: 6553-6556; Lemaitre, *et al.*, 1987. *Proc. Natl. Acad. Sci.* 84: 648-652; PCT Publication No. WO88/09810) or the blood-brain barrier (*see, e.g.*, PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (*see, e.g.*, Krol, *et al.*, 1988. *BioTechniques* 6:958-976) or intercalating agents (*see, e.g.*, Zon,

20 1988. *Pharm. Res.* 5: 539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, and the like.

GPCRX Polypeptides

A polypeptide according to the invention includes a polypeptide including the amino

25 acid sequence of GPCRX polypeptides whose sequences are provided in SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174,

30 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residues shown in SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26,

28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200 while still encoding a protein that maintains its GPCRX activities and physiological functions, or a functional fragment thereof.

In general, a GPCRX variant that preserves GPCRX-like function includes any variant in which residues at a particular position in the sequence have been substituted by other amino acids, and further include the possibility of inserting an additional residue or residues between two residues of the parent protein as well as the possibility of deleting one or more residues from the parent sequence. Any amino acid substitution, insertion, or deletion is encompassed by the invention. In favorable circumstances, the substitution is a conservative substitution as defined above.

One aspect of the invention pertains to isolated GPCRX proteins, and biologically-active portions thereof, or derivatives, fragments, analogs or homologs thereof. Also provided are polypeptide fragments suitable for use as immunogens to raise anti-GPCRX antibodies. In one embodiment, native GPCRX proteins can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, GPCRX proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, a GPCRX protein or polypeptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" polypeptide or protein or biologically-active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the GPCRX protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of GPCRX proteins in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly-produced. In one embodiment, the language "substantially free of cellular material" includes preparations of GPCRX proteins having less than about 30% (by dry weight) of non-GPCRX proteins (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-GPCRX proteins, still more preferably less than about 10% of non-GPCRX proteins, and most preferably less than about 5% of non-GPCRX proteins. When the GPCRX protein or biologically-active portion thereof is recombinantly-

produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the GPCRX protein preparation.

The language "substantially free of chemical precursors or other chemicals" includes preparations of GPCRX proteins in which the protein is separated from chemical precursors or other chemicals that are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of GPCRX proteins having less than about 30% (by dry weight) of chemical precursors or non-GPCRX chemicals, more preferably less than about 20% chemical precursors or non-GPCRX chemicals, still more preferably less than about 10% chemical precursors or non-GPCRX chemicals, and most preferably less than about 5% chemical precursors or non-GPCRX chemicals.

Biologically-active portions of GPCRX proteins include peptides comprising amino acid sequences sufficiently homologous to or derived from the amino acid sequences of the GPCRX proteins (*e.g.*, the amino acid sequence shown in SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200) that include fewer amino acids than the full-length GPCRX proteins, and exhibit at least one activity of a GPCRX protein. Typically, biologically-active portions comprise a domain or motif with at least one activity of the GPCRX protein. A biologically-active portion of a GPCRX protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acid residues in length.

Moreover, other biologically-active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native GPCRX protein.

In an embodiment, the GPCRX protein has an amino acid sequence shown in SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200. In other

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embodiments, the GPCRX protein is substantially homologous to SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140,

5   142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200, and retains the functional activity of the protein of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122,

10   124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200, yet differs in amino acid sequence due to natural allelic variation or mutagenesis, as described in detail, below. Accordingly, in another embodiment, the GPCRX protein is a protein that comprises an amino acid sequence at least about 45%

15   homologous to the amino acid sequence SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188,

20   190, 192, 194, 196, 198 and 200, and retains the functional activity of the SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174,

25   176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200.

Determining Homology Between Two or More Sequences

        To determine the percent homology of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be

30   introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or

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nucleotide as the corresponding position in the second sequence, then the molecules are homologous at that position (*i.e.*, as used herein amino acid or nucleic acid "homology" is equivalent to amino acid or nucleic acid "identity").

The nucleic acid sequence homology may be determined as the degree of identity between two sequences. The homology may be determined using computer programs known in the art, such as GAP software provided in the GCG program package. *See,* Needleman and Wunsch, 1970. *J Mol Biol* 48: 443-453. Using GCG GAP software with the following settings for nucleic acid sequence comparison: GAP creation penalty of 5.0 and GAP extension penalty of 0.3, the coding region of the analogous nucleic acid sequences referred to above exhibits a degree of identity preferably of at least 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 99%, with the CDS (encoding) part of the DNA sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199. The term "sequence identity" refers to the degree to which two polynucleotide or polypeptide sequences are identical on a residue-by-residue basis over a particular region of comparison. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over that region of comparison, determining the number of positions at which the identical nucleic acid base (*e.g.*, A, T, C, G, U, or I, in the case of nucleic acids) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the region of comparison (*i.e.*, the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The term "substantial identity" as used herein denotes a characteristic of a polynucleotide sequence, wherein the polynucleotide comprises a sequence that has at least 80 percent sequence identity, preferably at least 85 percent identity and often 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison region.

Chimeric and Fusion Proteins

The invention also provides GPCRX chimeric or fusion proteins. As used herein, a GPCRX "chimeric protein" or "fusion protein" comprises a GPCRX polypeptide operatively-

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linked to a non-GPCRX polypeptide. An "GPCRX polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a GPCRX protein (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104,

5   106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198 and 200), whereas a "non-GPCRX polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein that is not substantially homologous to the GPCRX protein, e.g., a protein that is

10   different from the GPCRX protein and that is derived from the same or a different organism. Within a GPCRX fusion protein the GPCRX polypeptide can correspond to all or a portion of a GPCRX protein. In one embodiment, a GPCRX fusion protein comprises at least one biologically-active portion of a GPCRX protein. In another embodiment, a GPCRX fusion protein comprises at least two biologically-active portions of a GPCRX protein. In yet

15   another embodiment, a GPCRX fusion protein comprises at least three biologically-active portions of a GPCRX protein. Within the fusion protein, the term "operatively-linked" is intended to indicate that the GPCRX polypeptide and the non-GPCRX polypeptide are fused in-frame with one another. The non-GPCRX polypeptide can be fused to the N-terminus or C-terminus of the GPCRX polypeptide.

20   In one embodiment, the fusion protein is a GST-GPCRX fusion protein in which the GPCRX sequences are fused to the C-terminus of the GST (glutathione S-transferase) sequences. Such fusion proteins can facilitate the purification of recombinant GPCRX polypeptides.

              In another embodiment, the fusion protein is a GPCRX protein containing a

25   heterologous signal sequence at its N-terminus. In certain host cells (e.g., mammalian host cells), expression and/or secretion of GPCRX can be increased through use of a heterologous signal sequence.

              In yet another embodiment, the fusion protein is a GPCRX-immunoglobulin fusion protein in which the GPCRX sequences are fused to sequences derived from a member of the

30   immunoglobulin protein family. The GPCRX-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a GPCRX ligand and a GPCRX protein on the surface of a cell, to thereby suppress GPCRX-mediated signal transduction in vivo. The GPCRX-

immunoglobulin fusion proteins can be used to affect the bioavailability of a GPCRX cognate ligand. Inhibition of the GPCRX ligand/GPCRX interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, as well as modulating (e.g. promoting or inhibiting) cell survival. Moreover, the GPCRX-immunoglobulin fusion

5   proteins of the invention can be used as immunogens to produce anti-GPCRX antibodies in a subject, to purify GPCRX ligands, and in screening assays to identify molecules that inhibit the interaction of GPCRX with a GPCRX ligand.

A GPCRX chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different

10   polypeptide sequences are ligated together in-frame in accordance with conventional techniques, e.g., by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional

15   techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., Ausubel, et al. (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are

20   commercially available that already encode a fusion moiety (e.g., a GST polypeptide). A GPCRX-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the GPCRX protein.

GPCRX Agonists and Antagonists

25   The invention also pertains to variants of the GPCRX proteins that function as either GPCRX agonists (i.e., mimetics) or as GPCRX antagonists. Variants of the GPCRX protein can be generated by mutagenesis (e.g., discrete point mutation or truncation of the GPCRX protein). An agonist of the GPCRX protein can retain substantially the same, or a subset of, the biological activities of the naturally occurring form of the GPCRX protein. An antagonist

30   of the GPCRX protein can inhibit one or more of the activities of the naturally occurring form of the GPCRX protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the GPCRX protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. In one

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embodiment, treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein has fewer side effects in a subject relative to treatment with the naturally occurring form of the GPCRX proteins.

Variants of the GPCRX proteins that function as either GPCRX agonists (*i.e.*,
5   mimetics) or as GPCRX antagonists can be identified by screening combinatorial libraries of mutants (*e.g.*, truncation mutants) of the GPCRX proteins for GPCRX protein agonist or antagonist activity. In one embodiment, a variegated library of GPCRX variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of GPCRX variants can be produced by, for example,
10   enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential GPCRX sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display) containing the set of GPCRX sequences therein. There are a variety of methods which can be used to produce libraries of potential GPCRX variants from a degenerate oligonucleotide sequence. Chemical
15   synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential GPCRX sequences. Methods for synthesizing degenerate oligonucleotides are well-known within the art. *See, e.g.,* Narang, 1983. *Tetrahedron* 39: 3;
20   Itakura, *et al.,* 1984. *Annu. Rev. Biochem.* 53: 323; Itakura, *et al.,* 1984. *Science* 198: 1056; Ike, *et al.,* 1983. *Nucl. Acids Res.* 11: 477.

Polypeptide Libraries

In addition, libraries of fragments of the GPCRX protein coding sequences can be
25   used to generate a variegated population of GPCRX fragments for screening and subsequent selection of variants of a GPCRX protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a GPCRX coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double-stranded
30   DNA that can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S_1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, expression libraries can

be derived which encodes N-terminal and internal fragments of various sizes of the GPCRX proteins.

Various techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of GPCRX proteins. The most widely used techniques, which are amenable to high throughput analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique that enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify GPCRX variants. *See, e.g.,* Arkin and Yourvan, 1992. *Proc. Natl. Acad. Sci. USA* 89: 7811-7815; Delgrave, *et al.,* 1993. *Protein Engineering* 6:327-331.

Anti-GPCRX Antibodies

Also included in the invention are antibodies to GPCRX proteins, or fragments of GPCRX proteins. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin (Ig) molecules, i.e., molecules that contain an antigen binding site that specifically binds (immunoreacts with) an antigen. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab}, $F_{ab'}$ and $F_{(ab')2}$ fragments, and an F_{ab} expression library. In general, an antibody molecule obtained from humans relates to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses as well, such as IgG_1, IgG_2, and others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain. Reference herein to antibodies includes a reference to all such classes, subclasses and types of human antibody species.

An isolated GPCRX-related protein of the invention may be intended to serve as an antigen, or a portion or fragment thereof, and additionally can be used as an immunogen to generate antibodies that immunospecifically bind the antigen, using standard techniques for polyclonal and monoclonal antibody preparation. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments of the antigen for use as

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immunogens. An antigenic peptide fragment comprises at least 6 amino acid residues of the amino acid sequence of the full length protein and encompasses an epitope thereof such that an antibody raised against the peptide forms a specific immune complex with the full length protein or with any fragment that contains the epitope. Preferably, the antigenic peptide

5   comprises at least 10 amino acid residues, or at least 15 amino acid residues, or at least 20 amino acid residues, or at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the protein that are located on its surface; commonly these are hydrophilic regions.

In certain embodiments of the invention, at least one epitope encompassed by the

10   antigenic peptide is a region of GPCRX-related protein that is located on the surface of the protein, e.g., a hydrophilic region. A hydrophobicity analysis of the huma GPCRX-related protein sequence will indicate which regions of a GPCRX-related protein are particularly hydrophilic and, therefore, are likely to encode surface residues useful for targeting antibody production. As a means for targeting antibody production, hydropathy plots showing regions

15   of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation. See, e.g., Hopp and Woods, 1981, *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle 1982, *J. Mol. Biol.* 157: 105-142, each of which is incorporated herein by reference in its entirety. Antibodies that are specific for one or more

20   domains within an antigenic protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

A protein of the invention, or a derivative, fragment, analog, homolog or ortholog thereof, may be utilized as an immunogen in the generation of antibodies that immunospecifically bind these protein components.

25   Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies directed against a protein of the invention, or against derivatives, fragments, analogs homologs or orthologs thereof (see, for example, Antibodies: A Laboratory Manual, Harlow and Lane, 1988, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, incorporated herein by reference). Some of these antibodies are

30   discussed below.

Polyclonal Antibodies

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For the production of polyclonal antibodies, various suitable host animals (e.g., rabbit, goat, mouse or other mammal) may be immunized by one or more injections with the native protein, a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, the naturally occurring immunogenic

5   protein, a chemically synthesized polypeptide representing the immunogenic protein, or a recombinantly expressed immunogenic protein. Furthermore, the protein may be conjugated to a second protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. The preparation can

10   further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (e.g., aluminum hydroxide), surface active substances (e.g., lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), adjuvants usable in humans such as Bacille Calmette-Guerin and Corynebacterium parvum, or similar immunostimulatory agents.

15   Additional examples of adjuvants which can be employed include MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

The polyclonal antibody molecules directed against the immunogenic protein can be isolated from the mammal (e.g., from the blood) and further purified by well known techniques, such as affinity chromatography using protein A or protein G, which provide

20   primarily the IgG fraction of immune serum. Subsequently, or alternatively, the specific antigen which is the target of the immunoglobulin sought, or an epitope thereof, may be immobilized on a column to purify the immune specific antibody by immunoaffinity chromatography. Purification of immunoglobulins is discussed, for example, by D. Wilkinson (The Scientist, published by The Scientist, Inc., Philadelphia PA, Vol. 14, No. 8

25   (April 17, 2000), pp. 25-28).

Monoclonal Antibodies

The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular

30   species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs thus

contain an antigen binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein, *Nature*, 256:495 (1975). In a hybridoma method, a mouse,

5   hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes can be immunized in vitro.

The immunizing agent will typically include the protein antigen, a fragment thereof or

10   a fusion protein thereof. Generally, either peripheral blood lymphocytes are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, MONOCLONAL ANTIBODIES: PRINCIPLES AND PRACTICE, Academic Press, (1986) pp.

15   59-103). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells can be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine

20   phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a

25   medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, *J. Immunol.*, 133:3001 (1984);

30   Brodeur et al., MONOCLONAL ANTIBODY PRODUCTION TECHNIQUES AND APPLICATIONS, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the antigen. Preferably, the binding

specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by

5   the Scatchard analysis of Munson and Pollard, *Anal. Biochem.*, 107:220 (1980). Preferably, antibodies having a high degree of specificity and a high binding affinity for the target antigen are isolated.

After the desired hybridoma cells are identified, the clones can be subcloned by limiting dilution procedures and grown by standard methods. Suitable culture media for this

10   purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells can be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclones can be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel

15   electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies can also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the

20   heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA

25   also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; Morrison, *Nature* 368, 812-13 (1994)) or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted

30   for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

Humanized Antibodies

The antibodies directed against the protein antigens of the invention can further comprise humanized antibodies or human antibodies. These antibodies are suitable for administration to humans without engendering an immune response by the human against the administered immunoglobulin. Humanized forms of antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')$_2$ or other antigen-binding subsequences of antibodies) that are principally comprised of the sequence of a human immunoglobulin, and contain minimal sequence derived from a non-human immunoglobulin. Humanization can be performed following the method of Winter and co-workers (Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. (See also U.S. Patent No. 5,225,539.) In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies can also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., 1986; Riechmann et al., 1988; and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)).

Human Antibodies

Fully human antibodies relate to antibody molecules in which essentially the entire sequences of both the light chain and the heavy chain, including the CDRs, arise from human genes. Such antibodies are termed "human antibodies", or "fully human antibodies" herein. Human monoclonal antibodies can be prepared by the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 Immunol Today 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be

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produced by using human hybridomas (see Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

5   In addition, human antibodies can also be produced using additional techniques, including phage display libraries (Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks et al., *J. Mol. Biol.*, 222:581 (1991)). Similarly, human antibodies can be made by introducing human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge,

10   human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in Marks et al. (*Bio/Technology* 10, 779-783 (1992)); Lonberg et al. (*Nature* 368 856-859 (1994)); Morrison (*Nature* 368, 812-13 (1994)); Fishwild et

15   al,(*Nature Biotechnology* 14, 845-51 (1996)); Neuberger (*Nature Biotechnology* 14, 826 (1996)); and Lonberg and Huszar (*Intern. Rev. Immunol.* 13 65-93 (1995)).

Human antibodies may additionally be produced using transgenic nonhuman animals which are modified so as to produce fully human antibodies rather than the animal's endogenous antibodies in response to challenge by an antigen. (See PCT publication

20   WO94/02602). The endogenous genes encoding the heavy and light immunoglobulin chains in the nonhuman host have been incapacitated, and active loci encoding human heavy and light chain immunoglobulins are inserted into the host's genome. The human genes are incorporated, for example, using yeast artificial chromosomes containing the requisite human DNA segments. An animal which provides all the desired modifications is then obtained as

25   progeny by crossbreeding intermediate transgenic animals containing fewer than the full complement of the modifications. The preferred embodiment of such a nonhuman animal is a mouse, and is termed the Xenomouse™ as disclosed in PCT publications WO 96/33735 and WO 96/34096. This animal produces B cells which secrete fully human immunoglobulins. The antibodies can be obtained directly from the animal after

30   immunization with an immunogen of interest, as, for example, a preparation of a polyclonal antibody, or alternatively from immortalized B cells derived from the animal, such as hybridomas producing monoclonal antibodies. Additionally, the genes encoding the immunoglobulins with human variable regions can be recovered and expressed to obtain the

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antibodies directly, or can be further modified to obtain analogs of antibodies such as, for example, single chain Fv molecules.

An example of a method of producing a nonhuman host, exemplified as a mouse, lacking expression of an endogenous immunoglobulin heavy chain is disclosed in U.S. Patent No. 5,939,598. It can be obtained by a method including deleting the J segment genes from at least one endogenous heavy chain locus in an embryonic stem cell to prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, the deletion being effected by a targeting vector containing a gene encoding a selectable marker; and producing from the embryonic stem cell a transgenic mouse whose somatic and germ cells contain the gene encoding the selectable marker.

A method for producing an antibody of interest, such as a human antibody, is disclosed in U.S. Patent No. 5,916,771. It includes introducing an expression vector that contains a nucleotide sequence encoding a heavy chain into one mammalian host cell in culture, introducing an expression vector containing a nucleotide sequence encoding a light chain into another mammalian host cell, and fusing the two cells to form a hybrid cell. The hybrid cell expresses an antibody containing the heavy chain and the light chain.

In a further improvement on this procedure, a method for identifying a clinically relevant epitope on an immunogen, and a correlative method for selecting an antibody that binds immunospecifically to the relevant epitope with high affinity, are disclosed in PCT publication WO 99/53049.

F_{ab} Fragments and Single Chain Antibodies

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an antigenic protein of the invention (see e.g., U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (see e.g., Huse, et al., 1989 Science 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for a protein or derivatives, fragments, analogs or homologs thereof. Antibody fragments that contain the idiotypes to a protein antigen may be produced by techniques known in the art including, but not limited to: (i) an $F_{(ab')2}$ fragment produced by pepsin digestion of an antibody molecule; (ii) an F_{ab} fragment generated by reducing the disulfide bridges of an $F_{(ab')2}$ fragment; (iii) an

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F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (iv) F_v fragments.

Bispecific Antibodies

5   Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for an antigenic protein of the invention. The second binding target is any other antigen, and advantageously is a cell-surface protein or receptor or receptor subunit.

10   Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities (Milstein and Cuello, *Nature*, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas)

15   produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, 1991 *EMBO J.*, 10:3655-3659.

Antibody variable domains with the desired binding specificities (antibody-antigen

20   combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the

25   immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., *Methods in Enzymology*, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers

30   which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or

similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

5   Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')$_2$ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., *Science* 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')$_2$ fragments.

10   These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB

15   derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

            Additionally, Fab' fragments can be directly recovered from E. coli and chemically coupled to form bispecific antibodies. Shalaby et al., *J. Exp. Med.* 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')$_2$ molecule. Each

20   Fab' fragment was separately secreted from E. coli and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

            Various techniques for making and isolating bispecific antibody fragments directly

25   from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., *J. Immunol.* 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody

30   heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., *Proc. Natl. Acad. Sci. USA* 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V$_H$) connected to a

light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody

5   fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., *J. Immunol.* 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., *J. Immunol.* 147:60 (1991).

Exemplary bispecific antibodies can bind to two different epitopes, at least one of

10   which originates in the protein antigen of the invention. Alternatively, an anti-antigenic arm of an immunoglobulin molecule can be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular antigen.

15   Bispecific antibodies can also be used to direct cytotoxic agents to cells which express a particular antigen. These antibodies possess an antigen-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the protein antigen described herein and further binds tissue factor (TF).

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Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells

25   (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360; WO 92/200373; EP 03089). It is contemplated that the antibodies can be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins can be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include

30   iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

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Effector Function Engineering

It can be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) can be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated can have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., J. Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity can also be prepared using heterobifunctional cross-linkers as described in Wolff et al. Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and can thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from Pseudomonas aeruginosa), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolaca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include ^{212}Bi, ^{131}I, ^{131}In, ^{90}Y, and ^{186}Re.

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates

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(such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for

5 conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody can be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is in turn

10 conjugated to a cytotoxic agent.

In one embodiment, methods for the screening of antibodies that possess the desired specificity include, but are not limited to, enzyme-linked immunosorbent assay (ELISA) and other immunologically-mediated techniques known within the art. In a specific embodiment, selection of antibodies that are specific to a particular domain of a GPCRX protein is

15 facilitated by generation of hybridomas that bind to the fragment of a GPCRX protein possessing such a domain. Thus, antibodies that are specific for a desired domain within a GPCRX protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

Anti-GPCRX antibodies may be used in methods known within the art relating to the

20 localization and/or quantitation of a GPCRX protein (e.g., for use in measuring levels of the GPCRX protein within appropriate physiological samples, for use in diagnostic methods, for use in imaging the protein, and the like). In a given embodiment, antibodies for GPCRX proteins, or derivatives, fragments, analogs or homologs thereof, that contain the antibody derived binding domain, are utilized as pharmacologically-active compounds (hereinafter

25 "Therapeutics").

An anti-GPCRX antibody (e.g., monoclonal antibody) can be used to isolate a GPCRX polypeptide by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-GPCRX antibody can facilitate the purification of natural GPCRX polypeptide from cells and of recombinantly-produced GPCRX polypeptide

30 expressed in host cells. Moreover, an anti-GPCRX antibody can be used to detect GPCRX protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the GPCRX protein. Anti-GPCRX antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g.,

to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials.

5   Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a

10   luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I, ^{131}I, ^{35}S or ^{3}H.

GPCRX Recombinant Expression Vectors and Host Cells

15   Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding a GPCRX protein, or derivatives, fragments, analogs or homologs thereof. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA

20   segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon

25   introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively-linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as

30   the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, that is operatively-linked to the nucleic acid

5 sequence to be expressed. Within a recombinant expression vector, "operably-linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner that allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell).

10 The term "regulatory sequence" is intended to includes promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Regulatory sequences include those that direct constitutive expression of a nucleotide sequence in many types of host cell

15 and those that direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including

20 fusion proteins or peptides, encoded by nucleic acids as described herein (*e.g.*, GPCRX proteins, mutant forms of GPCRX proteins, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of GPCRX proteins in prokaryotic or eukaryotic cells. For example, GPCRX proteins can be expressed in bacterial cells such as *Escherichia coli*, insect cells (using baculovirus

25 expression vectors) yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

30 Expression of proteins in prokaryotes is most often carried out in *Escherichia coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion

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vectors typically serve three purposes: (*i*) to increase expression of recombinant protein; (*ii*) to increase the solubility of the recombinant protein; and (*iii*) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the

5   recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith and Johnson, 1988. *Gene* 67: 31-40), pMAL (New England Biolabs, Beverly, Mass.) and pRIT5 (Pharmacia, Piscataway, N.J.) that fuse

10   glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amrann *et al.*, (1988) *Gene* 69:301-315) and pET 11d (Studier *et al.*, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990)

15   60-89).

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein. *See, e.g.*, Gottesman, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 119-128. Another strategy is to alter the

20   nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (*see, e.g.*, Wada, *et al.*, 1992. *Nucl. Acids Res.* 20: 2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the GPCRX expression vector is a yeast expression vector.

25   Examples of vectors for expression in yeast *Saccharomyces cerivisae* include pYepSec1 (Baldari, *et al.*, 1987. *EMBO J.* 6: 229-234), pMFa (Kurjan and Herskowitz, 1982. *Cell* 30: 933-943), pJRY88 (Schultz *et al.*, 1987. *Gene* 54: 113-123), pYES2 (Invitrogen Corporation, San Diego, Calif.), and picZ (InVitrogen Corp, San Diego, Calif.).

Alternatively, GPCRX can be expressed in insect cells using baculovirus expression vectors.

30   Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*, SF9 cells) include the pAc series (Smith, *et al.*, 1983. *Mol. Cell. Biol.* 3: 2156-2165) and the pVL series (Lucklow and Summers, 1989. *Virology* 170: 31-39).

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In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987. *Nature* 329: 840) and pMT2PC (Kaufman, *et al.*, 1987. *EMBO J.* 6: 187-195). When used in mammalian cells, the expression vector's control

5   functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, adenovirus 2, cytomegalovirus, and simian virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see, *e.g.*, Chapters 16 and 17 of Sambrook, *et al.*, MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring

10   Harbor, N.Y., 1989.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific

15   promoters include the albumin promoter (liver-specific; Pinkert, *et al.*, 1987. *Genes Dev.* 1: 268-277), lymphoid-specific promoters (Calame and Eaton, 1988. *Adv. Immunol.* 43: 235-275), in particular promoters of T cell receptors (Winoto and Baltimore, 1989. *EMBO J.* 8: 729-733) and immunoglobulins (Banerji, *et al.*, 1983. *Cell* 33: 729-740; Queen and Baltimore, 1983. *Cell* 33: 741-748), neuron-specific promoters (*e.g.*, the neurofilament

20   promoter; Byrne and Ruddle, 1989. *Proc. Natl. Acad. Sci. USA* 86: 5473-5477), pancreas-specific promoters (Edlund, *et al.*, 1985. *Science* 230: 912-916), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Pat. No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, *e.g.*, the murine hox promoters (Kessel and Gruss, 1990. *Science* 249:

25   374-379) and the α-fetoprotein promoter (Campes and Tilghman, 1989. *Genes Dev.* 3: 537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively-linked to a regulatory sequence in a manner that allows

30   for expression (by transcription of the DNA molecule) of an RNA molecule that is antisense to GPCRX mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen that direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or

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regulatory sequences can be chosen that direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be

5   determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes *see, e.g.,* Weintraub, *et al.,* "Antisense RNA as a molecular tool for genetic analysis," *Reviews-Trends in Genetics,* Vol. 1(1) 1986.

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and

10   "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

15   A host cell can be any prokaryotic or eukaryotic cell. For example, GPCRX protein can be expressed in bacterial cells such as *E. coli,* insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional

20   transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.,* DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in

25   Sambrook, *et al.* (MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate

30   the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (*e.g.,* resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Various selectable markers include those that confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid

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encoding a selectable marker can be introduced into a host cell on the same vector as that encoding GPCRX or can be introduced on a separate vector. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (e.g., cells that have incorporated the selectable marker gene will survive, while the other cells die).

5   A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (i.e., express) GPCRX protein. Accordingly, the invention further provides methods for producing GPCRX protein using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding GPCRX protein has been introduced) in a suitable

10   medium such that GPCRX protein is produced. In another embodiment, the method further comprises isolating GPCRX protein from the medium or the host cell.

Transgenic GPCRX Animals

        The host cells of the invention can also be used to produce non-human transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte

15   or an embryonic stem cell into which GPCRX protein-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous GPCRX sequences have been introduced into their genome or homologous recombinant animals in which endogenous GPCRX sequences have been altered. Such animals are useful for studying the function and/or activity of GPCRX protein and for

20   identifying and/or evaluating modulators of GPCRX protein activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA that is integrated into the genome

25   of a cell from which a transgenic animal develops and that remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, a "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous GPCRX gene has been altered by homologous recombination between the

30   endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, e.g., an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing GPCRX-encoding nucleic acid into the male pronuclei of a fertilized oocyte (e.g., by microinjection, retroviral infection) and allowing the oocyte to develop in a pseudopregnant female foster animal. The huma GPCRX cDNA sequences of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 can be introduced as a transgene into the genome of a non-human animal. Alternatively, a non-human homologue of the huma GPCRX gene, such as a mouse GPCRX gene, can be isolated based on hybridization to the huma GPCRX cDNA (described further supra) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably-linked to the GPCRX transgene to direct expression of GPCRX protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866; 4,870,009; and 4,873,191; and Hogan, 1986. In: MANIPULATING THE MOUSE EMBRYO, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the GPCRX transgene in its genome and/or expression of GPCRX mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene-encoding GPCRX protein can further be bred to other transgenic animals carrying other transgenes.

To create a homologous recombinant animal, a vector is prepared which contains at least a portion of a GPCRX gene into which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the GPCRX gene. The GPCRX gene can be a human gene (e.g., the cDNA of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189,

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191, 193, 195, 197 and 199), but more preferably, is a non-human homologue of a huma

GPCRX gene. For example, a mouse homologue of huma GPCRX gene of SEQ ID NOS:1,

3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53,

55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101,

5   103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137,

139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173,

175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 can be used to construct a

homologous recombination vector suitable for altering an endogenous GPCRX gene in the

mouse genome. In one embodiment, the vector is designed such that, upon homologous

10   recombination, the endogenous GPCRX gene is functionally disrupted (*i.e.*, no longer

encodes a functional protein; also referred to as a "knock out" vector).

Alternatively, the vector can be designed such that, upon homologous recombination,

the endogenous GPCRX gene is mutated or otherwise altered but still encodes functional

protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of

15   the endogenous GPCRX protein). In the homologous recombination vector, the altered

portion of the GPCRX gene is flanked at its 5'- and 3'-termini by additional nucleic acid of

the GPCRX gene to allow for homologous recombination to occur between the exogenous

GPCRX gene carried by the vector and an endogenous GPCRX gene in an embryonic stem

cell. The additional flanking GPCRX nucleic acid is of sufficient length for successful

20   homologous recombination with the endogenous gene. Typically, several kilobases of

flanking DNA (both at the 5'- and 3'-termini) are included in the vector. *See, e.g.*, Thomas, *et

al.*, 1987. *Cell* 51: 503 for a description of homologous recombination vectors. The vector is

ten introduced into an embryonic stem cell line (*e.g.*, by electroporation) and cells in which

the introduced GPCRX gene has homologously-recombined with the endogenous GPCRX

25   gene are selected. *See, e.g.*, Li, *et al.*, 1992. *Cell* 69: 915.

The selected cells are then injected into a blastocyst of an animal (*e.g.*, a mouse) to

form aggregation chimeras. *See, e.g.*, Bradley, 1987. In: TERATOCARCINOMAS AND

EMBRYONIC STEM CELLS: A PRACTICAL APPROACH, Robertson, ed. IRL, Oxford, pp.

113-152. A chimeric embryo can then be implanted into a suitable pseudopregnant female

30   foster animal and the embryo brought to term. Progeny harboring the homologously-

recombined DNA in their germ cells can be used to breed animals in which all cells of the

animal contain the homologously-recombined DNA by germline transmission of the

transgene. Methods for constructing homologous recombination vectors and homologous

recombinant animals are described further in Bradley, 1991. *Curr. Opin. Biotechnol.* 2: 823-829; PCT International Publication Nos.: WO 90/11354; WO 91/01140; WO 92/0968; and WO 93/04169.

In another embodiment, transgenic non-humans animals can be produced that contain selected systems that allow for regulated expression of the transgene. One example of such a system is the cre/loxP recombinase system of bacteriophage P1. For a description of the cre/loxP recombinase system, *See, e.g.*, Lakso, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae. See,* O'Gorman, *et al.*, 1991. *Science* 251:1351-1355. If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, *e.g.*, by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut, *et al.*, 1997. *Nature* 385: 810-813. In brief, a cell (*e.g.*, a somatic cell) from the transgenic animal can be isolated and induced to exit the growth cycle and enter G_0 phase. The quiescent cell can then be fused, *e.g.*, through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell (*e.g.*, the somatic cell) is isolated.

Pharmaceutical Compositions

The GPCRX nucleic acid molecules, GPCRX proteins, and anti-GPCRX antibodies (also referred to herein as "active compounds") of the invention, and derivatives, fragments, analogs and homologs thereof, can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Suitable carriers are described in the most

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recent edition of Remington's Pharmaceutical Sciences, a standard reference text in the field, which is incorporated herein by reference. Preferred examples of such carriers or diluents include, but are not limited to, water, saline, finger's solutions, dextrose solution, and 5% human serum albumin. Liposomes and non-aqueous vehicles such as fixed oils may also be used. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (i.e., topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringeability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of

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surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the

5   composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, a GPCRX protein or anti-GPCRX antibody) in the required amount in an appropriate

10   solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation are vacuum drying and

15   freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form

20   of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar

25   nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

30   For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

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Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid

5   derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention

10   enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides,

15   polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be

20   prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be

25   treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active

30   compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (see, e.g., U.S. Patent No. 5,328,470) or by

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stereotactic injection (*see, e.g.*, Chen, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 3054-3057). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector

5   can be produced intact from recombinant cells, *e.g.*, retroviral vectors, the pharmaceutical preparation can include one or more cells that produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

Screening and Detection Methods

10   The isolated nucleic acid molecules of the invention can be used to express GPCRX protein (*e.g.*, via a recombinant expression vector in a host cell in gene therapy applications), to detect GPCRX mRNA (*e.g.*, in a biological sample) or a genetic lesion in a GPCRX gene, and to modulate GPCRX activity, as described further, below. In addition, the GPCRX proteins can be used to screen drugs or compounds that modulate the GPCRX protein activity

15   or expression as well as to treat disorders characterized by insufficient or excessive production of GPCRX protein or production of GPCRX protein forms that have decreased or aberrant activity compared to GPCRX wild-type protein (*e.g.*; diabetes (regulates insulin release); obesity (binds and transport lipids); metabolic disturbances associated with obesity, the metabolic syndrome X as well as anorexia and wasting disorders associated with chronic

20   diseases and various cancers, and infectious disease(possesses anti-microbial activity) and the various dyslipidemias. In addition, the anti-GPCRX antibodies of the invention can be used to detect and isolate GPCRX proteins and modulate GPCRX activity. In yet a further aspect, the invention can be used in methods to influence appetite, absorption of nutrients and the disposition of metabolic substrates in both a positive and negative fashion.

25   The invention further pertains to novel agents identified by the screening assays described herein and uses thereof for treatments as described, *supra*.

Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for

30   identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, small molecules or other drugs) that bind to GPCRX proteins or have a stimulatory or inhibitory effect on, *e.g.*, GPCRX protein expression or GPCRX protein

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activity. The invention also includes compounds identified in the screening assays described herein.

In one embodiment, the invention provides assays for screening candidate or test compounds which bind to or modulate the activity of the membrane-bound form of a GPCRX protein or polypeptide or biologically-active portion thereof. The test compounds of the invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the "one-bead one-compound" library method; and synthetic library methods using affinity chromatography selection. The biological library approach is limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds. *See, e.g.,* Lam, 1997. *Anticancer Drug Design* 12: 145.

A "small molecule" as used herein, is meant to refer to a composition that has a molecular weight of less than about 5 kD and most preferably less than about 4 kD. Small molecules can be, *e.g.*, nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids or other organic or inorganic molecules. Libraries of chemical and/or biological mixtures, such as fungal, bacterial, or algal extracts, are known in the art and can be screened with any of the assays of the invention.

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt, *et al.*, 1993. *Proc. Natl. Acad. Sci. U.S.A.* 90: 6909; Erb, *et al.*, 1994. *Proc. Natl. Acad. Sci. U.S.A.* 91: 11422; Zuckermann, *et al.*, 1994. *J. Med. Chem.* 37: 2678; Cho, *et al.*, 1993. *Science* 261: 1303; Carrell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2059; Carell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2061; and Gallop, *et al.*, 1994. *J. Med. Chem.* 37: 1233.

Libraries of compounds may be presented in solution (*e.g.*, Houghten, 1992. *Biotechniques* 13: 412-421), or on beads (Lam, 1991. *Nature* 354: 82-84), on chips (Fodor, 1993. *Nature* 364: 555-556), bacteria (Ladner, U.S. Patent No. 5,223,409), spores (Ladner, U.S. Patent 5,233,409), plasmids (Cull, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 1865-1869) or on phage (Scott and Smith, 1990. *Science* 249: 386-390; Devlin, 1990. *Science* 249: 404-406; Cwirla, *et al.*, 1990. *Proc. Natl. Acad. Sci. U.S.A.* 87: 6378-6382; Felici, 1991. *J. Mol. Biol.* 222: 301-310; Ladner, U.S. Patent No. 5,233,409.).

In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of GPCRX protein, or a biologically-active portion thereof, on the

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cell surface is contacted with a test compound and the ability of the test compound to bind to a GPCRX protein determined. The cell, for example, can of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the GPCRX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic

5 label such that binding of the test compound to the GPCRX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with ^{125}I, ^{35}S, ^{14}C, or ^{3}H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish

10 peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of GPCRX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds GPCRX to form an assay mixture, contacting the assay mixture with a test

15 compound, and determining the ability of the test compound to interact with a GPCRX protein, wherein determining the ability of the test compound to interact with a GPCRX protein comprises determining the ability of the test compound to preferentially bind to GPCRX protein or a biologically-active portion thereof as compared to the known compound.

20   In another embodiment, an assay is a cell-based assay comprising contacting a cell expressing a membrane-bound form of GPCRX protein, or a biologically-active portion thereof, on the cell surface with a test compound and determining the ability of the test compound to modulate (e.g., stimulate or inhibit) the activity of the GPCRX protein or biologically-active portion thereof. Determining the ability of the test compound to modulate

25 the activity of GPCRX or a biologically-active portion thereof can be accomplished, for example, by determining the ability of the GPCRX protein to bind to or interact with a GPCRX target molecule. As used herein, a "target molecule" is a molecule with which a GPCRX protein binds or interacts in nature, for example, a molecule on the surface of a cell which expresses a GPCRX interacting protein, a molecule on the surface of a second cell, a

30 molecule in the extracellular milieu, a molecule associated with the internal surface of a cell membrane or a cytoplasmic molecule. A GPCRX target molecule can be a non-GPCRX molecule or a GPCRX protein or polypeptide of the invention. In one embodiment, a GPCRX target molecule is a component of a signal transduction pathway that facilitates

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transduction of an extracellular signal (e.g. a signal generated by binding of a compound to a membrane-bound GPCRX molecule) through the cell membrane and into the cell. The target, for example, can be a second intercellular protein that has catalytic activity or a protein that facilitates the association of downstream signaling molecules with GPCRX.

5   Determining the ability of the GPCRX protein to bind to or interact with a GPCRX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the GPCRX protein to bind to or interact with a GPCRX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by

10   detecting induction of a cellular second messenger of the target (i.e. intracellular Ca^{2+}, diacylglycerol, IP_3, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising a GPCRX-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, e.g., luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation,

15   or cell proliferation.

          In yet another embodiment, an assay of the invention is a cell-free assay comprising contacting a GPCRX protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to bind to the GPCRX protein or biologically-active portion thereof. Binding of the test compound to the GPCRX protein can be

20   determined either directly or indirectly as described above. In one such embodiment, the assay comprises contacting the GPCRX protein or biologically-active portion thereof with a known compound which binds GPCRX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a GPCRX protein, wherein determining the ability of the test compound to interact with

25   a GPCRX protein comprises determining the ability of the test compound to preferentially bind to GPCRX or biologically-active portion thereof as compared to the known compound.

          In still another embodiment, an assay is a cell-free assay comprising contacting GPCRX protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to modulate (e.g. stimulate or inhibit) the activity of the

30   GPCRX protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of GPCRX can be accomplished, for example, by determining the ability of the GPCRX protein to bind to a GPCRX target molecule by one of the methods described above for determining direct binding. In an alternative embodiment,

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determining the ability of the test compound to modulate the activity of GPCRX protein can be accomplished by determining the ability of the GPCRX protein further modulate a GPCRX target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as described, *supra.*

5　　　　In yet another embodiment, the cell-free assay comprises contacting the GPCRX protein or biologically-active portion thereof with a known compound which binds GPCRX protein to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a GPCRX protein, wherein determining the ability of the test compound to interact with a GPCRX protein comprises

10　　　determining the ability of the GPCRX protein to preferentially bind to or modulate the activity of a GPCRX target molecule.

　　　　The cell-free assays of the invention are amenable to use of both the soluble form or the membrane-bound form of GPCRX protein. In the case of cell-free assays comprising the membrane-bound form of GPCRX protein, it may be desirable to utilize a solubilizing agent

15　　　such that the membrane-bound form of GPCRX protein is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)$_n$, N-dodecyl--N,N-dimethyl-3-ammonio-1-propane

20　　　sulfonate, 3-(3-cholamidopropyl) dimethylamminiol-1-propane sulfonate (CHAPS), or 3-(3-cholamidopropyl)dimethylamminiol-2-hydroxy-1-propane sulfonate (CHAPSO).

　　　　In more than one embodiment of the above assay methods of the invention, it may be desirable to immobilize either GPCRX protein or its target molecule to facilitate separation of complexed from uncomplexed forms of one or both of the proteins, as well as to

25　　　accommodate automation of the assay. Binding of a test compound to GPCRX protein, or interaction of GPCRX protein with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtiter plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided that adds a domain that allows one or both

30　　　of the proteins to be bound to a matrix. For example, GST-GPCRX fusion proteins or GST-target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtiter plates, that are then combined with the test compound or the test compound and either the non-adsorbed target protein or GPCRX

protein, and the mixture is incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components, the matrix immobilized in the case of beads, complex determined either directly or indirectly, for example, as described,

5   supra. Alternatively, the complexes can be dissociated from the matrix, and the level of GPCRX protein binding or activity determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either the GPCRX protein or its target molecule can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated

10   GPCRX protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well-known within the art (e.g., biotinylation kit, Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with GPCRX protein or target molecules, but which do not interfere with binding of the GPCRX protein to its target

15   molecule, can be derivatized to the wells of the plate, and unbound target or GPCRX protein trapped in the wells by antibody conjugation. Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the GPCRX protein or target molecule, as well as enzyme-linked assays that rely on detecting an enzymatic activity

20   associated with the GPCRX protein or target molecule.

In another embodiment, modulators of GPCRX protein expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of GPCRX mRNA or protein in the cell is determined. The level of expression of GPCRX mRNA or protein in the presence of the candidate compound is compared to the level of expression of

25   GPCRX mRNA or protein in the absence of the candidate compound. The candidate compound can then be identified as a modulator of GPCRX mRNA or protein expression based upon this comparison. For example, when expression of GPCRX mRNA or protein is greater (i.e., statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of GPCRX mRNA or

30   protein expression. Alternatively, when expression of GPCRX mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of GPCRX mRNA or protein expression.

The level of GPCRX mRNA or protein expression in the cells can be determined by methods described herein for detecting GPCRX mRNA or protein.

In yet another aspect of the invention, the GPCRX proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (see, e.g., U.S. Patent No. 5,283,317;

5   Zervos, et al., 1993. Cell 72: 223-232; Madura, et al., 1993. J. Biol. Chem. 268: 12046-12054; Bartel, et al., 1993. Biotechniques 14: 920-924; Iwabuchi, et al., 1993. Oncogene 8: 1693-1696; and Brent WO 94/10300), to identify other proteins that bind to or interact with GPCRX ("GPCRX-binding proteins" or "GPCRX-bp") and modulate GPCRX activity. Such GPCRX-binding proteins are also likely to be involved in the propagation of

10   signals by the GPCRX proteins as, for example, upstream or downstream elements of the GPCRX pathway.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for GPCRX is fused to a

15   gene encoding the DNA binding domain of a known transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, in vivo, forming a GPCRX-dependent complex, the DNA-binding and activation

20   domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ) that is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene that encodes the protein which interacts with GPCRX.

25   The invention further pertains to novel agents identified by the aforementioned screening assays and uses thereof for treatments as described herein.

Detection Assays

Portions or fragments of the cDNA sequences identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide

30   reagents. By way of example, and not of limitation, these sequences can be used to: (i) map their respective genes on a chromosome; and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing);

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and (*iii*) aid in forensic identification of a biological sample. Some of these applications are described in the subsections, below.

Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. This process is called chromosome mapping. Accordingly, portions or fragments of the GPCRX sequences, SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199, or fragments or derivatives thereof, can be used to map the location of the GPCRX genes, respectively, on a chromosome. The mapping of the GPCRX sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, GPCRX genes can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the GPCRX sequences. Computer analysis of the GPCRX, sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the GPCRX sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (*e.g.*, human and mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow, because they lack a particular enzyme, but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. *See, e.g.,* D'Eustachio, *et al.,* 1983. *Science* 220: 919-924. Somatic cell hybrids containing only fragments of human

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chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the GPCRX sequences to design oligonucleotide primers, sub-localization can be achieved with panels of fragments from specific chromosomes.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical like colcemid that disrupts the mitotic spindle. The chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases, will suffice to get good results at a reasonable amount of time. For a review of this technique, *see,* Verma, *et al.*, HUMAN CHROMOSOMES: A MANUAL OF BASIC TECHNIQUES (Pergamon Press, New York 1988).

Reagents for chromosome mapping can be used individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found, *e.g.,* in McKusick, MENDELIAN INHERITANCE IN MAN, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, *e.g.,* Egeland, *et al.*, 1987. *Nature,* 325: 783-787.

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Moreover, differences in the DNA sequences between individuals affected and unaffected with a disease associated with the GPCRX gene, can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes, such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

Tissue Typing

The GPCRX sequences of the invention can also be used to identify individuals from minute biological samples. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. The sequences of the invention are useful as additional DNA markers for RFLP ("restriction fragment length polymorphisms," described in U.S. Patent No. 5,272,057).

Furthermore, the sequences of the invention can be used to provide an alternative technique that determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the GPCRX sequences described herein can be used to prepare two PCR primers from the 5'- and 3'-termini of the sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the invention can be used to obtain such identification sequences from individuals and from tissue. The GPCRX sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Much of the allelic variation is due to single nucleotide polymorphisms (SNPs), which include restriction fragment length polymorphisms (RFLPs).

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Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers that each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197 and 199 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

Predictive Medicine

The invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trials are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the invention relates to diagnostic assays for determining GPCRX protein and/or nucleic acid expression as well as GPCRX activity, in the context of a biological sample (e.g., blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant GPCRX expression or activity. The disorders include metabolic disorders, diabetes, obesity, infectious disease, anorexia, cancer-associated cachexia, cancer, neurodegenerative disorders, Alzheimer's Disease, Parkinson's Disorder, immune disorders, and hematopoietic disorders, and the various dyslipidemias, metabolic disturbances associated with obesity, the metabolic syndrome X and wasting disorders associated with chronic diseases and various cancers. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with GPCRX protein, nucleic acid expression or activity. For example, mutations in a GPCRX gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with GPCRX protein, nucleic acid expression, or biological activity.

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Another aspect of the invention provides methods for determining GPCRX protein, nucleic acid expression or activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or

5   prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of GPCRX in clinical trials.

10   These and other agents are described in further detail in the following sections.

Diagnostic Assays

An exemplary method for detecting the presence or absence of GPCRX in a biological sample involves obtaining a biological sample from a test subject and contacting

15   the biological sample with a compound or an agent capable of detecting GPCRX protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes GPCRX protein such that the presence of GPCRX is detected in the biological sample. An agent for detecting GPCRX mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to GPCRX mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length GPCRX

20   nucleic acid, such as the nucleic acid of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189,

25   191, 193, 195, 197 and 199, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to GPCRX mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

An agent for detecting GPCRX protein is an antibody capable of binding to GPCRX

30   protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')$_2$) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a

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detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently-labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with

5   fluorescently-labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect GPCRX mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of GPCRX mRNA include Northern

10   hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of GPCRX protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations, and immunofluorescence. *In vitro* techniques for detection of GPCRX genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of GPCRX protein include introducing into a subject a labeled anti-GPCRX

15   antibody. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a

20   peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting GPCRX protein, mRNA, or genomic DNA, such that the presence of GPCRX protein, mRNA or genomic DNA is detected in the biological sample, and

25   comparing the presence of GPCRX protein, mRNA or genomic DNA in the control sample with the presence of GPCRX protein, mRNA or genomic DNA in the test sample.

The invention also encompasses kits for detecting the presence of GPCRX in a biological sample. For example, the kit can comprise: a labeled compound or agent capable of detecting GPCRX protein or mRNA in a biological sample; means for determining the

30   amount of GPCRX in the sample; and means for comparing the amount of GPCRX in the sample with a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect GPCRX protein or nucleic acid.

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Prognostic Assays

The diagnostic methods described herein can furthermore be utilized to identify subjects having or at risk of developing a disease or disorder associated with aberrant

5   GPCRX expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or at risk of developing a disorder associated with GPCRX protein, nucleic acid expression or activity. Alternatively, the prognostic assays can be utilized to identify a subject having or at risk for developing a disease or disorder. Thus, the invention provides a

10   method for identifying a disease or disorder associated with aberrant GPCRX expression or activity in which a test sample is obtained from a subject and GPCRX protein or nucleic acid (*e.g.*, mRNA, genomic DNA) is detected, wherein the presence of GPCRX protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant GPCRX expression or activity. As used herein, a "test sample" refers to a

15   biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (*e.g.*, serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder

20   associated with aberrant GPCRX expression or activity. For example, such methods can be used to determine whether a subject can be effectively treated with an agent for a disorder. Thus, the invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant GPCRX expression or activity in which a test sample is obtained and GPCRX protein or nucleic acid is detected (*e.g.*, wherein

25   the presence of GPCRX protein or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant GPCRX expression or activity).

The methods of the invention can also be used to detect genetic lesions in a GPCRX gene, thereby determining if a subject with the lesioned gene is at risk for a disorder

30   characterized by aberrant cell proliferation and/or differentiation. In various embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion characterized by at least one of an alteration affecting the integrity of a gene encoding a GPCRX-protein, or the misexpression of the GPCRX gene. For example,

such genetic lesions can be detected by ascertaining the existence of at least one of: (*i*) a deletion of one or more nucleotides from a GPCRX gene; (*ii*) an addition of one or more nucleotides to a GPCRX gene; (*iii*) a substitution of one or more nucleotides of a GPCRX gene, (*iv*) a chromosomal rearrangement of a GPCRX gene; (*v*) an alteration in the level of a

5   messenger RNA transcript of a GPCRX gene, (*vi*) aberrant modification of a GPCRX gene, such as of the methylation pattern of the genomic DNA, (*vii*) the presence of a non-wild-type splicing pattern of a messenger RNA transcript of a GPCRX gene, (*viii*) a non-wild-type level of a GPCRX protein, (*ix*) allelic loss of a GPCRX gene, and (*x*) inappropriate post-translational modification of a GPCRX protein. As described herein, there are a large

10   number of assay techniques known in the art which can be used for detecting lesions in a GPCRX gene. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a

15   polymerase chain reaction (PCR) (*see, e.g.*, U.S. Patent Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (*see, e.g.*, Landegran, *et al.*, 1988. *Science* 241: 1077-1080; and Nakazawa, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 360-364), the latter of which can be particularly useful for detecting point mutations in the GPCRX-gene (*see*, Abravaya, *et al.*, 1995. *Nucl. Acids Res.* 23: 675-682).

20   This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (*e.g.*, genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers that specifically hybridize to a GPCRX gene under conditions such that hybridization and amplification of the GPCRX gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the

25   size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (*see,* Guatelli, *et al.*, 1990. *Proc. Natl. Acad. Sci. USA* 87: 1874-1878), transcriptional

30   amplification system (*see,* Kwoh, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 1173-1177); Qβ Replicase (*see,* Lizardi, *et al*, 1988. *BioTechnology* 6: 1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques

well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in a GPCRX gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (*see, e.g.,* U.S. Patent No. 5,493,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in GPCRX can be identified by hybridizing a sample and control nucleic acids, *e.g.*, DNA or RNA, to high-density arrays containing hundreds or thousands of oligonucleotides probes. *See, e.g.,* Cronin, *et al.*, 1996. *Human Mutation* 7: 244-255; Kozal, *et al.*, 1996. *Nat. Med.* 2: 753-759. For example, genetic mutations in GPCRX can be identified in two dimensional arrays containing light-generated DNA probes as described in Cronin, *et al., supra.* Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the GPCRX gene and detect mutations by comparing the sequence of the sample GPCRX with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert, 1977. *Proc. Natl. Acad. Sci. USA* 74: 560 or Sanger, 1977. *Proc. Natl. Acad. Sci. USA* 74: 5463. It is also contemplated that any of a variety of automated sequencing procedures can be utilized when performing the diagnostic assays (*see, e.g.,* Naeve, *et al.*, 1995. *Biotechniques* 19: 448), including sequencing by mass spectrometry (see, *e.g.*, PCT International Publication No. WO 94/16101; Cohen, *et al.*, 1996. *Adv. Chromatography* 36: 127-162; and Griffin, *et al.*, 1993. *Appl. Biochem. Biotechnol.* 38: 147-159).

Other methods for detecting mutations in the GPCRX gene include methods in which protection from cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes. *See, e.g.,* Myers, *et al.,* 1985. *Science* 230: 1242. In general, the art technique of "mismatch cleavage" starts by providing heteroduplexes of formed by

5   hybridizing (labeled) RNA or DNA containing the wild-type GPCRX sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent that cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and sample strands. For instance, RNA/DNA duplexes can be treated with RNase and DNA/DNA hybrids treated

10   with S_1 nuclease to enzymatically digesting the mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. *See, e.g.,* Cotton, *et al.,* 1988. *Proc.*

15   *Natl. Acad. Sci. USA* 85: 4397; Saleeba, *et al.,* 1992. *Methods Enzymol.* 217: 286-295. In an embodiment, the control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize mismatched base pairs in double-stranded DNA (so called "DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in

20   GPCRX cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches. *See, e.g.,* Hsu, *et al.,* 1994. *Carcinogenesis* 15: 1657-1662. According to an exemplary embodiment, a probe based on a GPCRX sequence, *e.g.,* a wild-type GPCRX sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is

25   treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. *See, e.g.,* U.S. Patent No. 5,459,039. In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in GPCRX genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type

30   nucleic acids. *See, e.g.,* Orita, *et al.,* 1989. *Proc. Natl. Acad. Sci. USA*: 86: 2766; Cotton, 1993. *Mutat. Res.* 285: 125-144; Hayashi, 1992. *Genet. Anal. Tech. Appl.* 9: 73-79. Single-stranded DNA fragments of sample and control GPCRX nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids

varies according to sequence, the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In one

5   embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in electrophoretic mobility. *See, e.g.*, Keen, *et al.*, 1991. *Trends Genet.* 7: 5.

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient

10   gel electrophoresis (DGGE). *See, e.g.*, Myers, *et al.*, 1985. *Nature* 313: 495. When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA. *See,*

15   *e.g.*, Rosenbaum and Reissner, 1987. *Biophys. Chem.* 265: 12753.

Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions that permit

20   hybridization only if a perfect match is found. *See, e.g.*, Saiki, *et al.*, 1986. *Nature* 324: 163; Saiki, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 6230. Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

25   Alternatively, allele specific amplification technology that depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization; *see, e.g.*, Gibbs, *et al.*, 1989. *Nucl. Acids Res.* 17: 2437-2448) or at the extreme 3'-terminus of one primer where,

30   under appropriate conditions, mismatch can prevent, or reduce polymerase extension (*see, e.g.*, Prossner, 1993. *Tibtech.* 11: 238). In addition it may be desirable to introduce a novel restriction site in the region of the mutation to create cleavage-based detection. *See, e.g.*, Gasparini, *et al.*, 1992. *Mol. Cell Probes* 6: 1. It is anticipated that in certain embodiments

amplification may also be performed using *Taq* ligase for amplification. *See, e.g.,* Barany, 1991. *Proc. Natl. Acad. Sci. USA* 88: 189. In such cases, ligation will occur only if there is a perfect match at the 3'-terminus of the 5' sequence, making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of amplification.

5   The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used, *e.g.,* in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving a GPCRX gene.

10   Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which GPCRX is expressed may be utilized in the prognostic assays described herein. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

15 **Pharmacogenomics**

      Agents, or modulators that have a stimulatory or inhibitory effect on GPCRX activity (*e.g.,* GPCRX gene expression), as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (The disorders include metabolic disorders, diabetes, obesity, infectious disease, anorexia, cancer-

20 associated cachexia, cancer, neurodegenerative disorders, Alzheimer's Disease, Parkinson's Disorder, immune disorders, and hematopoietic disorders, and the various dyslipidemias, metabolic disturbances associated with obesity, the metabolic syndrome X and wasting disorders associated with chronic diseases and various cancers.) In conjunction with such treatment, the pharmacogenomics (*i.e.,* the study of the relationship between an individual's

25 genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (*e.g.,* drugs) for prophylactic or therapeutic treatments based on a

30 consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of GPCRX protein, expression of GPCRX nucleic acid, or mutation content of GPCRX genes in

an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See e.g., Eichelbaum, 1996. *Clin. Exp. Pharmacol. Physiol.*, 23: 983-985; Linder, 1997. *Clin. Chem.*, 43: 254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body (altered drug action) or genetic conditions transmitted as single factors altering the way the body acts on drugs (altered drug metabolism). These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. At the other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of GPCRX protein, expression of GPCRX nucleic acid, or mutation content of GPCRX genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition,

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pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when

5   treating a subject with a GPCRX modulator, such as a modulator identified by one of the exemplary screening assays described herein.

Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or

10   activity of GPCRX (*e.g.*, the ability to modulate aberrant cell proliferation and/or differentiation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent determined by a screening assay as described herein to increase GPCRX gene expression, protein levels, or upregulate GPCRX activity, can be monitored in clinical trails of subjects exhibiting decreased GPCRX gene expression, protein

15   levels, or downregulated GPCRX activity. Alternatively, the effectiveness of an agent determined by a screening assay to decrease GPCRX gene expression, protein levels, or downregulate GPCRX activity, can be monitored in clinical trails of subjects exhibiting increased GPCRX gene expression, protein levels, or upregulated GPCRX activity. In such clinical trials, the expression or activity of GPCRX and, preferably, other genes that have

20   been implicated in, for example, a cellular proliferation or immune disorder can be used as a "read out" or markers of the immune responsiveness of a particular cell.

By way of example, and not of limitation, genes, including GPCRX, that are modulated in cells by treatment with an agent (*e.g.*, compound, drug or small molecule) that modulates GPCRX activity (*e.g.*, identified in a screening assay as described herein) can be

25   identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of expression of GPCRX and other genes implicated in the disorder. The levels of gene expression (*i.e.*, a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced,

30   by one of the methods as described herein, or by measuring the levels of activity of GPCRX or other genes. In this manner, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

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In one embodiment, the invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, protein, peptide, peptidomimetic, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (*i*) obtaining a pre-administration sample from a subject prior to administration of the agent; (*ii*) detecting the level of expression of a GPCRX protein, mRNA, or genomic DNA in the preadministration sample; (*iii*) obtaining one or more post-administration samples from the subject; (*iv*) detecting the level of expression or activity of the GPCRX protein, mRNA, or genomic DNA in the post-administration samples; (*v*) comparing the level of expression or activity of the GPCRX protein, mRNA, or genomic DNA in the pre-administration sample with the GPCRX protein, mRNA, or genomic DNA in the post administration sample or samples; and (*vi*) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of GPCRX to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of GPCRX to lower levels than detected, *i.e.*, to decrease the effectiveness of the agent.

Methods of Treatment

The invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant GPCRX expression or activity. The disorders include cardiomyopathy, atherosclerosis, hypertension, congenital heart defects, aortic stenosis, atrial septal defect (ASD), atrioventricular (A-V) canal defect, ductus arteriosus, pulmonary stenosis, subaortic stenosis, ventricular septal defect (VSD), valve diseases, tuberous sclerosis, scleroderma, obesity, transplantation, adrenoleukodystrophy, congenital adrenal hyperplasia, prostate cancer, neoplasm; adenocarcinoma, lymphoma, uterus cancer, fertility, hemophilia, hypercoagulation, idiopathic thrombocytopenic purpura, immunodeficiencies, graft versus host disease, AIDS, bronchial asthma, Crohn's disease; multiple sclerosis, treatment of Albright hereditary ostoeodystrophy, and other diseases, disorders and conditions of the like.

These methods of treatment will be discussed more fully, below.

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Disease and Disorders

Diseases and disorders that are characterized by increased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with

5 Therapeutics that antagonize (*i.e.*, reduce or inhibit) activity. Therapeutics that antagonize activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to: (*i*) an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; (*ii*) antibodies to an aforementioned peptide; (*iii*) nucleic acids encoding an aforementioned peptide; (*iv*) administration of antisense nucleic

10 acid and nucleic acids that are "dysfunctional" (*i.e.*, due to a heterologous insertion within the coding sequences of coding sequences to an aforementioned peptide) that are utilized to "knockout" endoggenous function of an aforementioned peptide by homologous recombination (*see, e.g.*, Capecchi, 1989. *Science* 244: 1288-1292); or (*v*) modulators (*i.e.*, inhibitors, agonists and antagonists, including additional peptide mimetic of the invention or

15 antibodies specific to a peptide of the invention) that alter the interaction between an aforementioned peptide and its binding partner.

Diseases and disorders that are characterized by decreased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with Therapeutics that increase (*i.e.*, are agonists to) activity. Therapeutics that upregulate activity

20 may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to, an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; or an agonist that increases bioavailability.

Increased or decreased levels can be readily detected by quantifying peptide and/or RNA, by obtaining a patient tissue sample (*e.g.*, from biopsy tissue) and assaying it *in vitro* for RNA or

25 peptide levels, structure and/or activity of the expressed peptides (or mRNAs of an aforementioned peptide). Methods that are well-known within the art include, but are not limited to, immunoassays (*e.g.*, by Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis, immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs (*e.g.*, Northern assays, dot

30 blots, *in situ* hybridization, and the like).

Prophylactic Methods

In one aspect, the invention provides a method for preventing, in a subject, a disease or condition associated with an aberrant GPCRX expression or activity, by administering to the subject an agent that modulates GPCRX expression or at least one GPCRX activity. Subjects at risk for a disease that is caused or contributed to by aberrant GPCRX expression or activity can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the GPCRX aberrancy, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending upon the type of GPCRX aberrancy, for example, a GPCRX agonist or GPCRX antagonist agent can be used for treating the subject. The appropriate agent can be determined based on screening assays described herein. The prophylactic methods of the invention are further discussed in the following subsections.

Therapeutic Methods

Another aspect of the invention pertains to methods of modulating GPCRX expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of GPCRX protein activity associated with the cell. An agent that modulates GPCRX protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of a GPCRX protein, a peptide, a GPCRX peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more GPCRX protein activity. Examples of such stimulatory agents include active GPCRX protein and a nucleic acid molecule encoding GPCRX that has been introduced into the cell. In another embodiment, the agent inhibits one or more GPCRX protein activity. Examples of such inhibitory agents include antisense GPCRX nucleic acid molecules and anti-GPCRX antibodies. These modulatory methods can be performed *in vitro* (*e.g.*, by culturing the cell with the agent) or, alternatively, *in vivo* (*e.g.*, by administering the agent to a subject). As such, the invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of a GPCRX protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (*e.g.*, an agent identified by a screening assay described herein), or combination of agents that modulates

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(*e.g.*, up-regulates or down-regulates) GPCRX expression or activity. In another embodiment, the method involves administering a GPCRX protein or nucleic acid molecule as therapy to compensate for reduced or aberrant GPCRX expression or activity.

Stimulation of GPCRX activity is desirable in situations in which GPCRX is abnormally downregulated and/or in which increased GPCRX activity is likely to have a beneficial effect. One example of such a situation is where a subject has a disorder characterized by aberrant cell proliferation and/or differentiation (*e.g.*, cancer or immune associated disorders). Another example of such a situation is where the subject has a gestational disease (*e.g.*, preclampsia).

Determination of the Biological Effect of the Therapeutic

In various embodiments of the invention, suitable *in vitro* or *in vivo* assays are performed to determine the effect of a specific Therapeutic and whether its administration is indicated for treatment of the affected tissue.

In various specific embodiments, *in vitro* assays may be performed with representative cells of the type(s) involved in the patient's disorder, to determine if a given Therapeutic exerts the desired effect upon the cell type(s). Compounds for use in therapy may be tested in suitable animal model systems including, but not limited to rats, mice, chicken, cows, monkeys, rabbits, and the like, prior to testing in human subjects. Similarly, for *in vivo* testing, any of the animal model system known in the art may be used prior to administration to human subjects.

Prophylactic and Therapeutic Uses of the Compositions of the Invention

The GPCRX nucleic acids and proteins of the invention are useful in potential prophylactic and therapeutic applications implicated in a variety of disorders including, but not limited to: metabolic disorders, diabetes, obesity, infectious disease, anorexia, cancer-associated cancer, neurodegenerative disorders, Alzheimer's disease, Parkinson's disorder, immune disorders, hematopoietic disorders, and the various dyslipidemias, metabolic disturbances associated with obesity, the metabolic syndrome X and wasting disorders associated with chronic diseases and various cancers.

As an example, a cDNA encoding the GPCRX protein of the invention may be useful in gene therapy, and the protein may be useful when administered to a subject in need thereof. By way of non-limiting example, the compositions of the invention will have

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efficacy for treatment of patients suffering from: metabolic disorders, diabetes, obesity, infectious disease, anorexia, cancer-associated cachexia, cancer, neurodegenerative disorders, Alzheimer's disease, Parkinson's disorder, immune disorders, hematopoietic disorders, and the various dyslipidemias.

5   Both the novel nucleic acid encoding the GPCRX protein, and the GPCRX protein of the invention, or fragments thereof, may also be useful in diagnostic applications, wherein the presence or amount of the nucleic acid or the protein are to be assessed. A further use could be as an anti-bacterial molecule (*i.e.,* some peptides have been found to possess anti-bacterial properties). These materials are further useful in the generation of antibodies which

10   immunospecifically-bind to the novel substances of the invention for use in therapeutic or diagnostic methods.

The invention will be further described in the following examples, which do not limit the scope of the invention described in the claims.

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP000818_D	1/2	CCATGAGGAATTTCTCGGTGGTGTCCGAATTCATCCTGCTGGGCATCCCTCACACGG AGGGTCTGGAGACTATTCTGTTGGTCCTGTTTTGTCCTTCTACATCTTCACCCTTAT GGGGAACCTGCTCATCTTGCTGCTATTGTCTCCTCCTGCTGGCTTCACACGCCCAT GTACTTCTTCCTGTCCAAGCTGTCTGTTTTGACCTATTTTCCCTTCTGTGAGTTCC CCTAAGATGCTGTGCTATCTTTCAGGGAACAGCCGAGCCATCTCCTATGCAGGCTGT GCATCCCAGCTCTTCTTCTACCATTTCCTGGGCTGCACTGAGTGTTTCCTGTACACG GTGATGGCCTACGACCGCTTTGTTGCCATTTGTCACCCTCTACGCTACACCATAATC ATGAGCCACAGAGCACATGTATCATCCTAGCCATGGGGACCTCATTCTTTGGCTGCATT CAGGCCACCTTCTGACCACTCTCAACTTCCAATTGCCTTACTGTGTCCCCAATGAG GTGGACTATTATTTCTGTGATATCCCAGTCATGCTGAAGCTGGCTTGTGCAGATACC TCAGCCCTGGAGATGGTGGGGGTTCATCAGTGTGGGCCTCATGCCCCCTCAGCTGTTTC CTTCTCATCCTCACCTCCTACAGTGGCATCGTCTTCTCCATCTTGGAGATCTGCTCTG CCGAGGGCCGACGCCGTGCCTTCTCCACCTGCAGCGCGCCACCTCCTGC TTTTTACATGCCAGTGGTCCTCCTCATTTACCTGAGGCTACCGAGGCCTACACCCACCAGCCTGGGTTGG ATGCAACTGTTCAAATTCTGAATAAACCTGGTCACCCCATGCTGAACCCCTTAATCT ACAGTCTCAGGAATAAGGAGGTGAAATTATCACTAAGGAAGGTCTTATATCAGCTG GGCTTCCTTCCTGAGCCAGTTGTAGAGAGAAATAA	MVKGNHSTVTEFNLAGLTD KPELQLPLFLLFLGIYVVTV VGNLSMITLIGFSSHLHTPM YHFLSSLSFIDLCQSSVITPK MLVNFVSERNIISYPACMTQ LYFFLVLVISECHMLAAMA YDHYIAICNPLLYHVAMSY QVCSWMVVEVYFMGFIGA TCSHSLHAKSAFLEGRCNQP LLLGSFPTTGALPLQYFYQR NSSLCFSAFNILFRSLTILSSY IFIVASILCIRSTEGRSKTFST CSSHISAVSVFFGSAAFMYL QPSSVSSMDQGSVFCVLCY CCAHAEPPIYSLRNKDVKV ALIKFLEKRSFL

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP000818_B	3/4	CCATGAGGAATTTCTCGGTGGTGTCCGAATTCATCCTGCTGGGCATCCCTCACACGG AGGGTCTGGAGACTATTCTGTTGGTCCTGTTTTTGTCCTTCTACATCTTCACCCTTAT GGGGAACCTGCTCATCTTGCTGGCTATTGTCTCCTCCTGCGCTTCACACGCCCAT GTACTTCTTCCTGTGCAAGCTGTCTGTTTTTGACCTATTTTCCCTTCTGTGAGTTCC CCTAAGATGCTGTGCTATCTTTCAGGGAACAGCCGAGCCATCCTATGCAGGCTGT GCATCCCAGCTCTTCTTCTACCATTTCCTGGGCTGCACTGAGTGTTTCCTGTACACG GTGATGGCCTACGACCGCTTTGTTGTGCCATTTGTCACCCTCTACGCTACACCATAATC ATGAGCCACAGAGCATGTATCATCCTAGCCATGGGGACCTCATTCTTTGGCTGCATT CAGGCCACCTTTCTGACCACTCCACCTTCCAATTGCCTTACTGTGTCCCCAATGAG GTGGACTATTATTTCTGTGATATCCCAGTCATGCTGAAGCTGGCTTGTGCAGATACC TCAGCCCTGGAGATGGTGGGGTTCATCAGTGTGGGCCTCATGCCCCTCAGCTGTTTC CTTCTCATCCTCACCTCCTACAGTGGCATGGCATGTCTTCTCCATCTTGGAGATCTGCTCTG CCGAGGGCCGACGCCGTGCCTCTCCACCTGCGCCACCTCACCGCCATCCTGC TTTTTACATGCCAGTGGTCCTCATTACCTGAGGCCTACCACCACAGCCTGGTTGG ATGCAACTGTTCAAATTCTGAATAAACCTGGTCACCCCCATGCTGAACCCCTTAATCT ACAGTCTCAGGAATAAGGAGGTGAAATTATCACTAAGGAAGGTCTTATATCAGCTG GGCTTCCTTCCTGAGCAGTTGTGAGAGAAATAA	MRNFSVVSEFILLGIPHTEGL ETILLVLFLSFYIFTLMGNLL ILLAIVSSARLHTPMYFFLCK LSVFDLFFPSVSSPKMLCYL SGNSRAISYAGCASQLFFYH FLGCTECFLYTVMAYDRFV AICHPLRYTIMSHRACIILA MGTSFFGCIQAIFLTLTFQ LPYCVPNEVDYYFCDIPVM LKLACADTSALEMVGFISV GLMPLSCFLLLTSYSGIVFSI LEICSAEGRRRAFSTCSAHL TAILLFYMPVVLIYLRPTHS LWLDATVQILNNLVTPMLN PLIYSLRNKEVKLSLRKVLY QLGFLPEQL

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Table 1

Acc. No.	SEQ ID NO (Nucl)/ SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP000818_A_2	5/6	CCATGAGGAATTTCTCGGTGGTGTCCGAATTCATCCTGCTGGGCATCCCTCACACGG AGGGTCTGGAGACTATTCTGTTGGTGCTGTTTTTGTCCTTCTACATCTTCACCCTTAT GGGGAACCTGCTCATCTTGCTGCTATTGTCTCCTCCTGCTCGGCTTCACACGCCCAT GTACTTCTTCCTGTGCAAGCTGTCTGTTTTTGACCTATTTTCCCTTCTGTGAGTTCC CCTAAGATGCTGTGCTATCTTTCAGGGAACAGCCGAGCCATCTCCATGCAGGCTGT GCATCCCAGCTCTTCTTCTACCATTTCCTGGGCTGCACTGAGTGTTTCCTGTACACG GTGATGGCCTACGACCGGCTTTGTTGCCATTTGTCACCCTCTACGCTACACCATAATC ATGAGCCACAGAGCAGCATGTATCATCCTAGCCATGGGACCTCATTCTTTGGCTGCATT CAGGCCACCTTTCTGACCACTCTCACCTTCCAATTGCCTTACTGTGTCCCAATGAG GTGGACTATTATTTCTGTGATATCCCAGTCATGCTCATGCTGAAGCTGGCTTGTGCAGATACC TCAGCCCTGGAGATGGTGGGGTTCATCAGTGTGGGCCCTCATGCCCCTGTTTC CTTCTCATCCTCACCTCCTACAGTGGCATCGTCTTCTCCATCTTGGAGATCTGCTCTG CCGAGGGCCGACGCCGTGCCTTCTCCACCTGCAGCGCCACCTCACCGCCATCCTGC TTTTTACATGCCAGTGGTCTCCTCATTTACCTGAGGCCTACCCACAGCCTGTGGTTGG ATGCAACTGTTCAAATTCTGAATAACCTGGTCACCCCATGCTGAACCCCTTAATCT ACAGTCTCAGGAATAAGGAGGTGAAATTATCACTAAGGAAGGTCTTATATCAGCTG GGCTTCCTTCCTGAGCAGTTGTAGAGAGAAATAA	MRNFSVVSEFILLGIPHTEGL ETILLVLFLSFYIFTLMGNLL ILLAIVSSARLHTPMYFFLCK LSVFDLFFPSVSSPKMLCYL SGNSRAISYAGCASQLFFYH FLGCTECFLYTVMAYDRFV AICHPLRYTIIMSHRACIILA MGTSFFGCIQATFLTTLTFQ LPYCVPNEVDYYFCDIPVM LKLACADTSALEMVGFISV GLMPLSCFLLJLTSYSGIVFSI LEICSAEGRRRAFSTCSAHL TAILLFYMPVVLIYLRPTHS LWLDATVQILNNLVTPMLN PLIYSLRNKEVKLSLRKVLY QLGFLPEQL

Table 1

Acc. No.	SEQ ID NO (Nucl)/ SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC011647_D	7/8	AAACCCTGATGGGGGGGCTTTGGGACTAACATCTCAAGTACTACCACCAGCTTCACTCTAA CAGGCTTCCCTGAGATGAAGGGTCTGGAGCACTGGCTGGCCCTTCTGCTGCTGC TTTATGCTATTTCCTTCCTGGCAACATCCTCATCCTCTTATCATAAAGGAAGAGC AGAGCTTGCACCAGCCAATGTACTACTTCCTGTCTCTTTTTCTGTTAATGACCTGG GTGTGTCCTTTTCTACATTGCCCCACTGTACTGGCTGCTGTGTTTCATGCCCCAGA GACAACTTTTGATGCCTGCCTGGCCCAGATGTTCTTCATCCACTTTCCTCCTGGAC AGAGTTTGGCATCCTACTGGCCATGAGTTTGACCACTATGTGGCCATCGTAACCC GCTGCGCTATGCCACAGTGCTCACTGATGTCCGTGGCCCACAATGGCATATCCAT TGTCATCCGCAGCTTCTGCATGGTATTCCCACTTCCCTCCTGAAGAGACTGCC TTTCTGTAAGGCCAGTGTGGTACTGGCCCATTCCTACTGTCTGCATGCAGACCTGAT TCGGCTGCCCTGGGGAGACACTACCATCAACAGCATGTATGGCCTGTTCATTGTCAT CTCTGCCTTTGGTGTGAGATTCACTGCTCATCCTCCTATGTGCTCATTCTACAT TCTGTGCTGGCCATTGCCTCCAGGGGTGAGAGGCTTAAGACACTCAACACATGTGT GTCACATATCTATGCAGTGCTGATCTTCTATGTGCCTATGGTTAGTGTGTCCATGGT TCATCGATTTGGGAGGCATGCTCCTGAATATGTGCACAAGTTCATGTCTCTTTGTAC CTCCAATGCTCTACCCAATTATCTATTCCATCAAGACTAAGGAGATTCGCGCAGGAGAC TACACAAGAT	MGGFGTNISSTTSFTLTGFP EMKGLEHWLAALLLLYAI SFLGNILILFIIKEEQSLHQPM YYFLSLFSVNDLGVSFSTLP TVLAAVCFHAPETTFDACL AQMFFIHFSSWTEFGILLAM SFDHYVAICNPLRYATVLTD VRVAHNGISIVIRSFCMVFP LPFLLKRLPFCKASVVLAHS YCLHADLIRLPWGDTTINS MYGLFIVISAFGVDSLLILLS YVLILHSVLAIASRGERLKT LNTCVSHIYAVLIFYVPMVS VSMVHRFGRHAPEYVHKF MSLCTSNALPNYLFHQD

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC011654_A	9/10	TAAATGTTGGGGAATTACTCTAGCGGCCACTGAATTTTTCTCTTAGGCTTCCCTGGC TCCCAAGAAGTATGCCGTATCCTATTTGCGACCTTCTTCCTCTTGTATGCAGTGACA GTGATGGGAAACGTGGTCATCATCACTGTCTGTGTTGATAAATGTCTGCAGTCC CCCATTTATTTTTCCTGGGCCACCTCTGTCCTGGAGATCCTGATCACATCCACC GCTGTCCCTTTATGCTCTGGGGGTTGCTGCTTCCAAGCACCCAGATCATGTCTTTG ACAGCCTGCTGCACAGCTATATTTATACCTTTCTTTGGGTACCTTGGAGTTGGCA TTAATGGGAGTGATGGCTGTGGACCGTTATGTGGCTGTGTGTAACCCTTTGAGGTA CAACATCATTATGAACAGCAGCACCTCATTTGGGTGATAATTGTGTCATGGGTTTT GGGGTTTCTTTCTGAAATCTGGCCAGTTTATGCCACTTTCAGCTTCTTCTGCAA ATCAAGTGTGTTAGATCATTTTATTGTGACCGAGGACAATTGCTCAAGGTATCCTG TGAGGACACTCTTTTCAGAGAGTTTATTCTTTTTCTAATGGCTGTTTTCATTATCATT GGTTCTTTGATCCCTACGATTGTCTCCTACACTACATCATCTCCACCAACCTCAAG ATTCCGTCAGCCTCTGGCTGGAGGAAATCCTTTCCACCTGTGCCTCCCACTTCACC TATGTTGTGATTGGCTATGGCAGCTGCTGTTTCTCTACGTGAAACCCAAGGAAACG CAGGCAGCCGAGTATAACAGGGTAGTGTCACTGGTGTTTAGTGGTGGTGACCCCTTTT CTGAACCCTTTTATCTTCACCCTGAGGAATGACAAATTCATACAGGCCTTTGGAGAT GGCATGAAACACTGCTATAAACTCCTTAAAAATTAA	MLGNYSSATEFFLLGFPGSQ EVCRILFATFFLLYAVTVMG NVVIIITVCVDKCLQSPIYFF LGHLCVLEILITSTAVPFML WGLLLPSTQIMSLTACAAQ LYLYLSLGTLELALMGVMA VDRYVAVCNPLRYNIIMNS STFIWVIIVSWVLGFLSEIWP VYATFQLTFCKSSVLDHFY CDRGQLLKVSCEDTLFREFI LFLMAVFIIIGSLIPTIVSYTY IISTNLKIPSASGWRKSFSTC ASHFTYVVIGYGSCLFLYVK PKETQAAEYNRVVSLLVLV VTPFLNPFIFTLRNDKFIQAF GDGMKHCYKLLKN

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC004977_A	11/12	GTGCTTTCCTTGGGTATGCTGGACCCCAGTAGTATTTCCAGTCACACTCTTTATCTCCAC TCTCTGTTTCCTCAGGGATTGAGAAAGGGACAATGTGGCAGAAGAATCAGACCTC TCTGGCAGACTTCATCCTTGAGGGGCTCTTCGATGACTCCCTTACCCACCTTTTCCTT TTCTCCTTGACCATGGTGGTCTTCCTTATTGCGGTGGCAACACCCTCACCATT CTCCTCATCTGCATTGATCCCCAGCTTCATCACACCAATGTATTTCCTGCTCAGCCAG CTCCCCTCATGGATCTGATGCATGTCTCCACAACCATCCTGAAGATGGCTACCAAC TACCTATCTGGCAAGAAATCTATCTCCTTTGTGGGCGTGTGCAACCCAGCACTTCCTC TATTTGTGTCTAGGTGGTGCTGAATGTTTTCTTAGCTGTCTCATGTCCTATGACCGCT ATGTTGCCATCTGTCATCCACTGCGCTATGGTTGGGGGCATCGTGAACTCCCTAATTCACATGG TGATGATGGCTGTCATGTCATGGTTGGGGGCCTGGAAGTTCCTCGGAAAGTTCTACTGTG CGATCTTGATGCACTTCCCTTTCTGTGGGCCTCGGAAAGTTCTACCACTTCTACTGTG AGTTCCCAGCTGTTGTGAAGTTGGTATGTGGGCGACATCACTGTGTATGAGACCACA GTGTACATCAGCAGCATTCTCCTCCTCCCCATCTTCCTGATTTCTACATCCTATG TCTTCATCCTTCAAAGTGTCATTCAGATGCGCTCATCTGGGAGCAAGAAATGCCT TTGCCACTTGTGCTCCCACCTTGGTTTCTCTTTGGTTGGTGCTGCATCTT CTCCTACATGAGACCCAGGTCCCAGTGCACTCTATTGCAGAACAAAGTTGGTTCTGT GTTCTACAGCATCATTACGCCCACCATTGAATTCTCTGATTTATACTCTCCGGAATAA AGATGTAGCTAGCTAAGGCTCTGAGAAGAGTGCTGAGGAGAGATGTTATCACCCAGTGCA TTCAACGACTGCAATTGTGGTTGCCCCGAGTGTAGA	MLDPSISSHTLYLHSLFPQG LRKGTMWQKNQTSLADFIL EGLFDDSLTHLFLFSLTMVV FLIAVSGNTLTLLICIDPQLH TPMYFLLSQLSLMDLMHVS TTILKMATNYLSGKKSISFV GCATQHFLYLCLGGAECFL LAVMSYDRYVAICHPLRYA VLMNKKVGLMMAVMSWL GASVNSLIHMAILMHFPFCG PRKVYHFYCEFPAVVKLVC GDITVYETTVYISSILLLLPIF LISTSYVFILQSVIQMRSSGS KRNAFATCGSHLTVVSLWF GACIFSYMRPRSQCTLLQNK VGSVFYSIITPTLNSLIYTLR NKDVAKALRRVLRRDVITQ CIQRLQLWLPRV

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC011904_A	13/14	TCTCTCGTTTCCTCAGGGATTGAGAAAGGGGACAATGTGGCAGAAGAATCAGACCTC TCTGGCAGACTTCATCCTTGAGGGGCTCTTCGATGACTCCCTTACCCACCTTTCCTT TTCTTCCTTGACCATGGTGGTCTTCCTTATTGGGGTGAGTGGCAACACCCTCACCATT CTCCTCATCTGCATTGATCCCCCAGCTTCATACACCAATGTATTTCCTGCTCAGCCAG CTCTCCCTCATGATCTGATGCATGTCCACAATCATCCTGAAGATGGCTACCAAC TACCTATCTGGCAAGAAATCTATCTCCTTTGTGGGCTGTGCAACCCAGCACTTCCTC TATTTGTGTCTAGGTGGTGCTGAAATGTTTTCTTAGCTGTGTCATGTCCTATGACCGCT ATGTTGCCATCTGTCATCCACTGCGCTATGCTGTGTCTCATGAACAAGAAGGTGGGAC TGATGATGGCTGTGTCATGTCATGGTTGGGGGCATCCGTGAACTCCCTAATTCACATGG CGATCTTGATGCACTTCCCTTTCTGTGGGCCTCGGAAAGTCTACCACTTCTACTGTG AGTTCCCAGCTGTTGTGAAGTTGGTATGTGGGCGACATCACTGTGTATGAGACCACA GTGTACATCAGCAGCATTCTCCTCCTCCCCATCTTCCTGATTTCTACATCCTATG TCTTCATCCTTCAAAGTGTCATTCAGATGCGCTCATCTGGGAGCAAGAGAAATGCCT TTGCCACTTGTGGCTCCCCACCTCACGGTGGTTTCCTTTGGTGGTGGCCTGCATCTT CTCCTACATGAGACCCAGGTCCCAGTGCACTCTATTGCAGAACAAAGTTGGTTCTGT GTTCTACAGCATCATTACGCCCACATTGAATTCTCTGATTTATACTCTCCGGAATAA AGATGTAGCTAAGGCTCTGAGAAGAGTGCTGAGGAGAGATGTTTATCACCCAGTGCA TTCAACGACTGCAATTGTGGTTGCCCCGAGTGTAGA	MWQKNQTSLADFILEGLFD DSLTHLFLFSLTMVVFLIAV SGNTLTILLICIDPQLHTPMY FLLSQLSLMDLMHVSTIILK MATNYLSGKKSISFVGCAT QHFLYLCLGGAECFLLAVM SYDRYVAICHPLRYAVLMN KKVGLMMAVMSWLGASV NSLIHMAILMHFPFCGPRKV YHFYCEFPAVVKLVCGDIT VYETTVYISSILLLPIFLIST SYVFILQSVIQMRSSGSKRN AFATCGSHLTVVSLWFGAC IFSYMRPRSQCTLLQNKVGS VFYSIITPTLNSLIYTLRNKD VAKALRVLRRDVITQCIQR LQLWLPRV

95

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
SC120295344_A	15/16	GGGACAATGTGGCAGAAGAATCAGACCTCTCTGGCAGACTTCATCCTTGAGGGGCT CTTCGATGACTCCCTTACCCACCTTTTCCTTTCTCCTTGACCATGGTGGTCTTCCTT ATTGCGGTGAGTGGCAACACCCTCACCATTCTCCTCATCTGCATTGATCCCCAGCTT CATACACCAATGTATTTCCTGCTCAGCCAGCTCTCCCTCATGGATCTGATGCATGTC TCCACAACCATCCTGAAGATGGCTACCAACTACCTATCTGGCAAGAAATCTATCTCC TTTGTGGGCTGTGCAACCCAGCACTTCCTCTATTTGTGTCTAGGTGGTGCTGAATGT TTTCTCTTAGCTGTCATGTCCTATGACCGCTATGTTGCCATCTGTCATCCACTGCGCT ATGCTGTGCTCATGAACAAGAAGGTGGGACTGATGGCTGTGCTCATGTCATGGTTG GGGGCATCCGTGAACTCCCTAATTCACATGGCGATCTTGATGCACTTCCCTTTCTGT GGGCCTCCGAAAGTCTACCACTTCTACTGTGAGTTCCCAGCTGTTGTGAAGTTGGTA TGTGGCGACATCACTGTGTATGAGACCACAGTGTACATCAGCAGCATTCTCCTCCTC CTCCCCATCTTCCTGATTTCTACATCCTATGTCTTCATCCTTCAAAGTGTCATTCAGA TGCGCTCATCTGGGAGCAAGAGAAATGCCTTTGCCACTTGTGGCTCCCACCTCACGG TGGTTTCTCTTTGGTTTGGTGCCTGCATCTTCCTCCTACATGAGACCCAGGTCCCAGT GCACTCTATTGCAGAACAAAGTTGGTTCGTTCTGTGTTCTACAGCATCATTACGCCCACAT TGAATTCTCTGATTTATACTCTCCGGAATAAAGATGTAGCTAAGGCTCTGAGAAGA GTGCTGAGGAGGAGATGTTATCACCCAGTGCATTCAACGACTGCAATTGTGGTTGCC CCGAGTGTAGAGTGGAATAG	MWQKNQTSLADFILEGLFD DSLTHLFLFSLTMVVFLIAV SGNTLTILICIDPQLHTPMY FLLSQLSLMDLMHVSTTILK MATNYLSGKKSISFVGCAT QHFLYLCLGGAECFLLAVM SYDRYVAICHPLRYAVLMN KKVGLMMAVMSWLGASV NSLIHMAILMHFPFCGPRKV YHFYCEFPAVVKLVCGDIT VYETTVYISSILLLPIFLIST SYVFILQSVIQMRSSGSKRN AFATCGSHLTVVSLWFGAC IFSYMRPRSQCTLLQNKVGS VFYSIITPTLNSLIYTLRNKD VAKALRRVLRRDVITQCIQR LQLWLPRV

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001804_H	17/18	AATGACTGTCAAAAGTCATTCTATAGTGACAGAGTTCAGTCTCAGGGGATTAACGA AGCAGCCAGATCTCCAGCTCTTTCACTTCCTCATTTCCTTGATATCCATATGGTCAC AATGGTGGGGAACTTGGGCATGATCACTCTAATTGTCTTAACTCTCAGCTTCACAC CCCCATGTACTACTTCTTCAGCAATCTGTCACTCTTGGATCTCTGCTATTCCTCCATT ACTAAACCCTAAGATGCTGGTGAACTTTGTGTTAAAGAAGAGCATTATCTCTTATGCA GGGTACACATGTCAAAGTTCTCACTTTTTCCTGGTTTTTGTCATTGCTAGGTGTTACATG CTGATGGTGAAGGCCTGTGACCACTATGTTGCCATCTGCTGCCCTTTGCTTTGCAAC GTCATCATGTCTCATGTCACCTGCTCCCTGATGGTGGCTGTGCTACACCATGGGA CTCGTTGTCTCCACAATAGAGACTGGGCTCATATTAAAACTGCCCTATTGTGAACTC CTCACCAGTCGCTGCTTCTGTGACATCCTCCCTCATGAAACTCTCCCGATCTAGT GCCTATGATGTTGAGATGGCAGTCTTCTTTTTTGCTAGATTCAACCTGAGAATCATG ATCTTAACAGTTCTTGTTTCTTACACCTTCATTCTCTTCAGCATCCTGCACATCAGCA CCACTGAGGGCAGGTCCAAAGTCTTCAGCAACCTGCAGCTTCCACCTTGCAGCTATAG GGATGTTCCATGGAAAGACTGCATTCAGGTACTTAAAACCCGCCATAACCAGTTCC CTGGCCCAAGAGAATGTGGCCTCTGTGTTCTACACTACAGTAATCTACGTGCCGAAT CCCCTAATGTACAGCCTGAAAAACAAGGATGTAAAAGCTGCCATGCAGAAAAACACT AAGGAGTAAGTTTTGTTGCAGATGTAATTATCTTGAGTTGCTAATCAACCCAATACA GTATCAATATAGGAAAGAAGCTTTCTGGAGATTTACAAAACCATAAGTGGCTTTCC TTCCAATTTTCTAGTA	MTVKSHSIVTEFSLRGLTKQ PDLQLFHFLIFLDIHMVTMV GNLGMITLICLNSQLHTPMY YFFSNLSLLDLCYSSITNPK MLVNFVLKKSIISYAGYMS KFYFFLVFVIARCYMLMVK ACDHYVAICCPLLCNVIMSH VTCSLMVAVVYTMGLVVS TIETGLILKLPYCELLTSRCF CDILPLMKLSRSSAYDVEM AVFFFARFNLRIMILTVLVS YTFILFSILHISTTEGRSKVFS TCSFHLAAIGMFHGKTAFR YLKPAITSSLAQENVASVFY TTVIYVPNPLMYSLKNKDV KAAMQKTLRSKFCCRCNYL ELLINPIQYQYRKEAFWRFT KP

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC005143_A	19/20	AATGGCACCTGGAAATGGCTCTTTCGTGACTGAATTCATTCTGGCGGGATTAACACA TCAGCCAGATCTCCAGTCCCCCTCGTTTCTTCCTGTTTCTAGTAATCTATGTGGTCACT CTGTTGGGAAACTTGGGCTTGGTAACTCTAATTGGGCTGAACTCACACCTTCATACC CCCATGTACTTCTTCCTCTTTAACTTGTCCTTCATAGATCTCGTTATTCTTCTGTGT TTATACCCAAAATGCTAATGAACTTTATTTCAGAGAAGAATATTATGTCCTTCAAGG GGTGCATGACCAACTTTCCTTTTCCCGATTTTTTGGTCATTTCTGAAGGTTATGTG CCGACGTCAATGGCGTATGATCGCTGTGGCCATCTGTACCCCACTTCTGTATCACAT TGCCATGTCTCCTACAGTGTGCTCCAGCCTTATGTTTGGTTCCTATTTGATGCCTTTT TCTGGTGCCATGGCCCACACTGGATGCATGCTGAGACTGACTTTCTGTGATGCGAAC ACCATCGATCACTACTTCTGTGACATCCTCCCCTCGCTCTCCTGCACCAGC ACCTACATCAATGAGCTGGTGGTTTCACTGTGGTTGGCATCAACATCATTGTGCCC ACTGTTACCATCTTTATCTCTTATGGTTTCATCCTCTCCAGCATCCTCCATATCAGTT CCAAGGAGGGCAGGTCCAAAGCTTCAGCACTTGCAGTTCCCATATAATTGCTGTTT CTCTGTTCTTTGGATCAGGTGCATTTATGTATCTCAACCCATCTTCTGCTGGGTCCAT GGATAAGAGAAAATTATCTTCTGTCTTTTATACAAATGTGGTTCCCATGTTGAACCC CTTAATCTACAGCCTGAGGAACAAAGATGTTAAATTTGCCCTAAGAAAAGCCCTGA GTAGTAGGAAACTTTGATAA	MAPGNGSFVTEFILAGLTHQ PDLQSPLFFLFLVIYVVTLLG NLGLVTLIGLNSHLHTPMYF FLFNLSFIDLCYSSVFIPKML MNFISEKNIMSFKGCMTQLS FSRFFWSFLKVMCRRQWR MIAVAICTPLLYHIAMSPTV CSSLMFGSYLMPFSGAMAH TGCMLRLTFCDANTIDHYF CDILPLLQLSCTSTYINELVV FTVVGINIIVPTVTIFISYGFI LSSILHISSKEGRSKAFSTCS SHIIAVSLFFGSGAFMYLNPS SAGSMDKRKLSSVFYTNVV PMLNPLIYSLRNKDVKFALR KALSSRKL

98

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001804_J	21/22	AATGGCACCTGGAAATGGCTCTTTCGTGACTGAATTCATTCTGGCGGGATTAACACA TCAGCCAGATCTCCAGTCCCCTCGTTCTTCCTGTTTCTCAGTAATCTATGTGGTCACT CTGTTGGGAAACTTGGGCTTGGTAACTCTAATTGGGCTGAACTCACACCTTCATACC CCCATGTACTTCTTCCTCTTTAACTTGTCCTTCATAGATCTCTGTTATTCTTCTGTGT TTACACCCAAAATGCTAATGAACTTTATTTCAGAGAAGAATATTATCTCCTTCAAGG GGTGCATGACCCAACTTTTCTTTTTCTGTTTTTTTGGTCATTTCTGAATGTTATGTG CCGACGTCAATGGCGTATGATCGCTGTGGCCATCTGTAACCCACTTCTGTATCACAT TGCCATGTCTCCTACAGTGTGCTCCCACACTGGATGCATGCTGAGAACTGACTTTCTT TCTGGTGCCATGGCCCACACTACTTCTGTGACATCCTCCCCTGCTCCGCTCCTGCACCAGC ACCATCGATCACTACTTCTGTGACATCATGTGGCATCAACATCATTGTGCCC ACCTACATCAATGAGCTGGTTTTCATCTCTTATGGTTTCATCCTCCAGCATCCTCCATATCAGTT ACTGTTACCATCTTTATCTCTTTATGGTTTCATCCTCCAGCATCCTCCATATAATTGCTGTTT CCAAGGAGGGCAGGTCCAAAGCTTTCAGCACTTGCAGTTCCCATATAATTGCTGTTT CTCTGTTCTTTGGATCAGGTGCATTTATGTATCTCAACCCATCTTCTGCTGGGTCCAT GGATAAGAGAAAATTATCTTCTGTCTTTTATACAAAATGTGGTTCCCATGTTGAACCC CTTAATCTACAGCCTGAGGAACAAAGATGTTAAATTTGCCCTAAGAAAAGCCCTGA GTAGTAGGAAACTTTGATAA	MAPGNGSFVTEFILAGLTHQ PDLQSPLFLFLVIYVVTLLG NLGLVTLIGLNSHLHTPMYF FLFNLSFIDLCYSSVFTPKML MNFISEKNIISFKGCMTQLFF FCFFWSFLNVMCRRQWRMI AVAICNPLLYHIAMSPTVCS SLMFGSYLMAFSGAMAHTG CMLRLTFCDANTIDHYFCDI LPLLQLSCTSTYINELVVFT VVGINIIVPTVTIFISYGFILSS ILHISSKEGRSKAFSTCSSHII AVSLFFGSGAFMYLNPSSAG SMDKRKLSSVFYTNVVPML NPLIYSLRNKDVKFALRKAL SSRKL

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001804_G	23/24	AATGGCACCTGGAAATGGCTCTTTCGTGACTGAATTCATTCTGGCGGGATTAACACA TCAGCCAGATCTCCAGTCCCCTCGTTCTTCCTGTTTCTAGTAATCTATGTGGTCACT CTGTTGGGAAACTTGGCGTTGGTAACTCTAATTGGGCTGAACTCACACCTTCATACC CCCATGTACTTCTTCCTCTTAACTTGTCCTTCATAGATCTCTGTTATTCTTCTGTGT TTACACCCAAAATGCTAATGAACTTTATTTCAGAGAGAAGAAATATTATCTCCTTCAAGG GGTGCATGACCCAACTTTCTTTTTCTGTTTTTTGGTCATTTCTGAATGTTATGTG CCGACGTCAATGGCGTATGATCGGCGTGTGGCCATCTGTAACCCACTTCTGTATCACAT TGCCATGTCTCCTACAGTGTGCTCCAGCCTTATGTTTGGTTCCTATTTGATGGCCTTT TCTGGTGCCATGGCCCACACTGGATGCATGCTGAGACTGACTTTCTGTGATGCGAAC ACCATCGATCACTACTTCTGTGACATCCTCCCCTCTCCAGCTCCTCGCCACCAGC ACCTACATCAATGAGCTGGTGGTTTCACTGTGGTTGGCATCAACATCATTGTGCCC ACTGTTACCATCTTTATCTCTTATGGTTTCATCCTCTCCAGCATCCTCCATATCAGTT CCAAGGAGGGCAGGTCCAAAGCTTTCAGCACTTGCAGTTCCCATATAAATTGCTGTTT CTCTGTTCTTTGGATCAGGTGCATTTATGTATCTCAACCCATCTTCTGCTGGGTCCAT GGATAAGAGAAAATTATCTTCTGTCTTTTATACAAATGTGGTTCCCATGTTGAACCC CTTAATCTACAGCCTGAGGAACAAAGATGTTAAATTTGCCCTAAGAAAGCCCTGA GTAGTAGGAAACTTTGATAA	MAPGNGSFVTEFILAGLTHQ PDLQSPLFLFLVIYVTLLG NLGLVTLJGLNSHLHTPMYF FLFNLSFIDLCYSSVFTPKML MNFISEKNIISFKGCMTQLFF FCFFWSFLNVMCRRQWRMI AVAICNPLLYHIAMSPTVCS SLMFGSYLMAFSGAMAHTG CMLRLTFCDANTIDHYFCDI LPLLQLSCTSTYINELVVFT VVGINIIVPTVTIFISYGFILSS ILHISSKEGRSKAFSTCSSHII AVSLFFGSGAFMYLNPSSAG SMDKRKLSSVFYTNVVPML NPLIYSLRNKDVKFALRKAL SSRKL

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001804_C	25/26	AATGGCACCTGAAAATGGCTCTTTCGTGACTGAATTCATTCTGGCGGGATTAACACA TCAGCCAGATCTCCAGTCCCCTCGTTCTTCCGTTTCTAGTAATCTATGTGGTCACT CTGTTGGGAAACTTGGGCTTGGTAACTCTAATTGGGCTGAACTCACACCTTCATACC CCCATGTACTTCTTCCTCTTAACTTGTCCTTCATAGATCTCGTTATTCTTCTGTGT TTACACCCAAAATGCTAATGAACTTTATTTCAGAGAAGAATATTATCTCCTTCAAGG GGTGCATGACCCAACTTTTCTTTTCTGTTTTTTTGGTCATTTCTGAAATGTTATGTG CCGACGTCAATGGCGTATGATCGCGTGTGGCCATCTGTAACCCACTTCTGTATCACAT TGCCATGTCTCCTACAGTGTGCTCCAGCCTTATGTTTGGTTCCTATTTGATGGCCTTT TCTGGTGCCATGGCCCCACACTGGATGCATGCTGAGACTTTCTGTGATGCGAAC ACCATCGATCACTACTTCTGTGACATCCTCCCTGCTCCGCTCCTGCACCAGC ACCTACATCAATGAGCTGGTGGTTTTCACTGGTTGGCATCAACATCATTGTGCCC ACTGTTACCATCTTTATCTCTTATGGTTTCATCTCTCCAGCATCCTCCATATCAGTT CCAAGGAGGGCAGGTCCAAAGCTTTCAGCACTTGCAGTTCCCATCATTGCTGTTT CTCTGTTCTTTGGATCAGGTGCATTTATGTATCTCAACCCATCTTCTGCTGGGTCCAT GGATAAGAAAATTATCTTCTGTGTCTTTATACAAAATGTGGTTCCCATGTTGAACCC CTTAATCTACAGCCTGAGGAACAAAGATGTTAAATTTGCCCTAAGAAAAGCCCTGA GTAGTAGGAAACTTTGATAA	MAPGNGSFVTEFILAGLTHQ PDLQSPLFFLFLVIYVVTLLG NLGLVTLIGLNSHLHTPMYF FLFNLSFIDLCYSSVFTPKML MNFISEKNIISFKGCMTQLFF FCFFWSFLNVMCRRQWRMI AVAICNPLLYHIAMSPTVCS SLMFGSYLMAFSGAMAHTG CMLRLTFCDANTIDHYFCDI LPLLQLSCTSTYINELVVFT VVGINIIVPTVTIFISYGFILSS ILHISSKEGRSKAFSTCSSHII AVSLFFGSGAFMYLNPSSAG SMDKRKLSSVFYTNVVPML NPLIYSLRNKDVKFALRKAL SSRKL

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001804_B	27/28	ACAAAAAATGCTGGCTAGAAACAACTCCTTAGTGACTGAATTTATTCTTGCTGGATT AACAGATCATCCAGAGTTCCAGCAACCCCTCTTTTCCTGTTTCTAGTGGTCTACAT TGTCACCATGGTAGGCAACCTTGGCTTGATCATTCTTTTCGGTCTAAATTCTCACCT CCACACACCAATGCTACTATTTCCTCTTCAATCTCTCCTTCAATCTCTGTTACTCC TCTGTTTTCACTCCCAAAATGCTAATGAACTTTGTATCAAAAAAGAATATTATCTCC TATGTTGGGTGCATGACTCAGCTGTTTTTCTTTCTTTTTGTCATCTCTGAATGTT ACATGTTGACCTCAATGGCATATGATCGCTATGTGGCCATCTGTAATCCATTGCTGT ATAAGGTCACCATGTCCCATCAGGTCTGTTCTATGCTCACTTTGCTGCTTACATAA TGGGATTGGCTGGAGCCACGGCCCACACCGGGTGCATGCTTAGACTCACCTTCTGC AGTGCTAATATCATCAACCATTACTTGTGTGACATACTCCCCCCTCCTCCAGCTTTCCT GCACCAGCACCTATGTCAACGAGGTGGTTGTTCTCATTGTTGTGGGTATTAATATCA TGGTACCCAGTTGTACCATCCTCATTTCTTATGTTTCATTGTCACTAGCATTCTTCA TATCAAATCCACTCAAGGAAGATCAAAAGCCTTCAGTACTTGTAGCTCTCATGTCAT TGCTCTGTCTCTGTTTTTGGGTCAGCGGCATTCAGTATTAAATATTCTTCTGGA TCTATGGAGCAGGAAAAGTTTCTTCGTGTTTTTCTACACTAATGTGGTGCCCATGCTC AATCCTCTCATCTACACAGTTTGAGGAACAAGGATGTCAAAGTTGCACTGAGGAAAGC TCTGATTAAAATTCAGAGAGAAGAAATATATTCTAATTAGAAGCA	MLARNNSLVTEFILAGLTD HPEFQQPLFLFLVVYIVTM VGNLGLIILFGLNSHLHTPM YYFLFNLSFIDLCYSSVFTPK MLMNFVSKKNIISYVGCMT QLFFLFFVISECYMLTSMA YDRYVAICNPLLYKVTMSH QVCSMLTFAAYIMGLAGAT AHTGCMLRLTFCSANIINHY LCDILPLLQLSCTSTYVNEV VVLIVVGINIMVPSCTILISY VFIVTSILHIKSTQGRSKAFS TCSSHVIALSLFFGSAAFMYI KYSSGSMEQGKVSSVFYTN VVPMLNPLIYSLRNKDVKV ALRKALIKIQRRNIF

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC011711_1	29/30	CTCACCATGCCACACCTCAGCAACACCACCACATCTGAGTTCCCAATCTTCCTCCTAACA GGCTTCCCTGGGCTGGAGGCCTTCCACATCTGGATCTCAATTCCCTTCTTCCTTCTG AGCACAGTTGCTCTCTTAGGGAACAGCATGATCCTATTGGTTGTTATTCTGGAGCCA AACCTCCATGAACCCATGTACTGTTTTCTTCATGCTGTCTGCCGCTGACCTGGGG CTGACCCTCTCCACAATGCCCACGACCCTCAGTGTCCTCTGGTTCAGTGCACGTGAA ATCATCCTCAATGCATGTATCATCCAGCTCTTTTCCTCCACAGCTCTGGCTTTATGG AATCCTCAGTACTGATGGCCATGGCTTTGACCGCTTTGTTGCCATTGCAGACCCC TCAGATATGCTACCATCCTGACAGACTCCAGAATTCTAAAGATTGGTGTAGCAATA GTCCTAAGAACATTGATCAGCCTCTTCTCCATCCCTCTTTCTCATTAAGAGACTGTCA TTTTGCAAAGTCAATGTCCTTTCCCATTCTTACTGCTTCCACCCTGATGCGCTTAAAG TTGCATGTTCTGATTCAAGGATGAACAGCTATGGAGGCTTAGCTGTTCTCATTCTGG TCACCGGGGTTGGTACACCATGTGTTGCGCTTTCCTACATCCTGATAATCCACTCTG TACTAAACATCATCTCTTCAGAGGGACGGAGGAAGGCCTTCGACACTTGTGGATCT CACATTGGGCAGTTGCAGTTCACCAATGTCCACCCACTATTGTCCAACATCTATTT AGATTTTTCCACAAGGCTTCACCAATAGTCCACCCACTATTGTCCAACATCTATTT CCTTGGCCCCTCTCGGCTGAACCCCATCATATATAGT	MPHLSNTTSEFPIFLLTGFPG LEAFHIWISIPFLLSTVALL GNSMILLVILEPNLHEPMY CFLFMLSAADLGLTLSTMPT TLSVLWFSAREIILNACIIQL FFLHSSGFMESSVLMAMAF DRFVAICRPLRYATILTDSRI LKIGVAIVLRTLISLSPSLFLI KRLSFCKVNVLSHSYCFHP DALKVACSDSRMNSYGGLA VLILVTGVGTPCVALSYILII HSVLNIISSEGRRKAFDTCG SHIGAVAVFYIPWVVLSVV HRFFHKASPICPPTIVQHLFP WPLSAEPHHI

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC009642_C	31/32	AAATCATGACTTTGGTTTCTTTTTCTTTTCCTCCTCCAAGCCATTGATAAATGCTCCT TAGCAATTCAAGCTGGAGGCTATCCCAGCCTTCTTTTCTCCTGGTAGGGATTCCAGG TTTAGAGGAAAGCCAGCACTGGATTGCACTGCCCCTGGGCATCCTTTACCTCCTTGC TTTAGTGGGCAATGTTACCATTCTCTTCATCATCTGGATGGACCCATCCTTGCACCA ATCTATGTACCTCTTCCTGTCCATGCCAGCTCCATCGACCTGGTTCTGGCCTCCTCC ACTGCACCCAAAGCCCTTGCAGTGCTCCTGGTTCATGCCCACGAGATTGGGTACATC GTCTGCCTGATCCAGATGTTCTTCATCCATGCATTCTCCTCCATGGAGTCAGGGGTA CTTGTGGCCATGGCTCTGGATCGCTATGTAGCCATTTGTCACCCCTTGCACCATTCC ACAATCCTGCATCCAGGGGTCATAGGGCGCATCGGAATGGTGGTGCTGGTGAGGGG ATTACTACTCCTTATCCCCTTCCCCATTTGTTGGGAACACTTATCTTCTGCCAAGCC ACCATCATAGGCCATGCTATTGTGAACATATGGCTGACTATGGCCTTGTGATTGGGCT GAAACCACAGTCAATCGAGCTTATGGGCTGACTATGCCCACATCCTCCAGCAGTGCTGAAGGT GGATGTTCTGGCCATTGGTGTTCCTATGCCCACATCCTCCAGCAGTGCTGAAGGT ACCAGGGAGTGAGGCCCGACTTAAGGCGTTAGCACATGTGGCTCTCATATTTGTG TCATCCTGGTCTTCTATGTCCCTGGAATTTCTCCTCCTTCCTCACTCACCGCTTGGTCA TCATGTACCCCATCATGTCCATGTTCTCTGGCCACACGGTATCTCCTCATGCCACCT GCGCTCAATCCTCCTTGTCTTGTCTATGGAGTGAAGACTCAGCAGATCCGCCAGCGAGTGCT CAGAGTGTTTACACAAAAGGATTGATCTGAACATATTCTCATT	MNLDSFFSFLLKSLIMALSN SSWRLPQPSFFLVGIPGLEES QHWIALPLGILYLLALVGNV TILFIIWMDPSLHQSMYLFLS MLAAIDLVVASSTAPKALA VLLVRAQEIGYTVCLIQMFF THAFSSMESGVLVAMALDR YVAICHPLHHSTILHPGVIG HIGMVVLVRGLLLLIPFLILL RKLIFCQATIIGHAYCEHMA VVKLACSETTVNRAYGLTV ALLVVGLDVLAIGVSYAHIL QAVLKVPGNEARLKAFSTC GSHVCVILVFYIPGMFSFLT HRFGHHVPHHVLLAILY RLVPPALNPLVYRVKTQKIH QGVLRVFTLKD

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC009758_A	33/34	GTGACCTTCCCTGGGCATGACAACCCACAACTCCACTGGTAGCAGCCACTCACTCTT CATTCTGCTGAGCATTCCTGGCTTAGAAGACCAGCACACATGGATGTCTCTCCCCTT CTTTATTTCCTACCTTGTTGCTTTCCTTGGGAACAGCCTCATCATCTTCATCATCATC ACTGAAATGCAGCCTCCACGAACCCATGTACCTTTCTCTGCTGGCTGTGGCT GACCTTATCCTGTCTACTACCACTGTGCCCAAGGCCCTAGCCATATTTGGTTCTAT GCTGGAGCAATATCCCTGGTGGCTGTGTTACCCAAATCTTCTTTATCCATGCTACC TTCATCGAGGAATCAGGAATTCTGTTGGCGATGGCACTGACCGCTATGTGGCCATC TGTGATCCACTGCACTATACCACAGTCGTCGTGTGCAAAAATCACAAAGATTGG CTTGGCTGTGTCCTGAGAAGCTTCTGTGTGATCATGCCAGATGTGTTTCTGGTAAA GCGGCTGCCTTTCTGCGCCATAGCAATCTGCTGCCACATACCTACTGTGAGCACATGGC TGTTGCCAAGTTTGCTTGTGCTGATATTCATGTCAATGTTTGGTATGGCTTGTCTGT CCTTCTCTATACTGTAGTGCTAGATGCCTTGCTTATCTTAGTGTCCTATAGCTTCATC CTGTATACAGGCTTCCACCTCCCCTCCCCAAGGAGCTCGGCAAAAGGCTCGGGCA CATGTGGCTCCCACCTCAGAGTCATTTCCATGTTCTACTTGCCTGGTATTTTTACCAT AATTACCCAGCGGTTTGGGCACCACCATTCTCCTCCCATACACACACATTCTGCTGGCCAA TGTCTGCGTGTTGGCTCCTCCCATGCTGAACCCCATCATTTATGGGATCAACACCAG GCAGATTCAAGAGTGTGTGTGCCAGTCTTTGTCCTCACAGAGGAAATGATGCTAGA TTTGACTAATCTGATAGTATGTTTATCACTATAGGGCTTTGCTTTCATTAGA	MTTHNSTGSSHSLFILLSIPG LEDQHTWMSLPFFISYLVAF LGNSLIIFIIITECSLHEPMYL FLCMLAVADLILSTTVPKA LAIFWFYAGAISLGGCVTQI FFIHATFIEESGILLAMALDR YVAICDPLHYTTVLSRAKIT KIGLAVVLRSFCVIMPDVFL VKRLPFCHSNLLPHTYCEH MAVAKFACADIHVNVWYG LSVLLYTVVLDALLILVSYS FILYTGFHLPSPRSSAKGSG HMWLPPQSHFHVLLAWYF YHNYPAVWAPCSSPYTHSA GQCLRVGSSHAEPHHLWDQ HQADSRVCAQSFVLTEEMM LDLTNLIVCLSL

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL358773_A	35/36	ATTACTCCTGCAATAATGGCAAATCTCACAATCGTGACTGAATTTATCCTTATGGGG TTTTCTACCAATAAAATATGTGCATTTGCATTTGGATTCTCTTCTTGTTGATTTATT TGTGTGCCCTGATGGGGAATGTCCTCCATTATCATGATCACAACTTTGGACCATCATC TCCACACCCGTGTATTTCTTCTTGAAGAATCTATCTTTCTTGGATCTCTGCCTTAT TTCAGTCACGGCTCCCAAATCTATCGCCAATTCTTTGATACACAACAACTCCATTTC ATTCCTTGGCTGTGTTTCCCAGGTCTTTTGTTGCTTCTTCAGCATCTGCAGAGCTG CTCCTCCTCACGGTGATGTCCTTGACCGGCTATATGTCACCCTCTGCACT ATGATGTCATCATGGACAGGAGCACCTGTGTCCAAAGAGCCACTGTGTCTTGGCTG TATGGGGTCTGATTGCTGTGATGCACACAGCTGGCACCTTCTCCTTATCCTACTGT GGGTCCAACATGGTCCATCAGTTCTTCTGTGACATTCCCCAGTTATTAGCTATTTCT TGCTCAGAAAATTTAATAAGAGAAATTGCACTCATCCTTATTAATGTAGTTTTTGGAT TTCTGCTGTTTATTGTCATCATCATTACCTATGTCCACGTCTTCTCTACAGTCAAGA AGATCCCTTCCACAGAAGGCCAGTCAAAAGCCTACTCTCTATTTGCCTTCCACACTTGC TGGTTGTGTTATTTCTTTCCCACTGGATTCATTGCTGTAATTTCTGTGTTCTACACTAGT CTCCTTCTATTTTGGATGCTGTAATTTCTGTGTTCTCACACTATGCTGCCCCAACCTT TAATCCCATTATATACAGTTTGAGAAACAAGGCCATAAAGGTGGCTCTGGGGATGT TGATAAAGGGAAAGCTCACCAAAAAGTAAAAGCT	MANLTIVTEFILMGFSTNKN MCILHSILFLLIYLCALMGN VLIIMITTLDHHLHTPVYFFL KNLSFLDLCLISVTAPKSIAN SLIHNNSISFLGCVSQVFLLL SSASAELLLTVMSFDRYTA ICHPLHYDVIMDRSTCVQR ATVSWLYGGLIAVMHTAGT FSLSYCGSNMVHQFFCDIPQ LLAISCSENLIREIALILNVV LDFCCFIVIIITYVHVFSTVK KIPSTEGQSKAYSICLPHLLV VLFLSTGFIAYLKPASESPSI LDAVISVFYTMLPPTFNPIIY SLRNKAIKVALGMLIKGKLT KK

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002512_G	37/38	ATAATGGTACGAAATACTTCTACACATATTTCATGGCCAAAACCAATAATTCAGAA GTTACTGAATTCATCCTCTGGGACTCACAGACAATCCAGAGCTCCAAGCCCTTTTT TAGGGGGATCTTTCTAGTGATCAATTAAGTAGTGTCATGGGTAGCCTTGGGTTAAT TATGCTAATTCATATCAGTCCTCAGCTTCACACAGCTATGTATTTTTTCTCAGCCAC GTAGCTTTTGTTTATTTTTGCTACACCTCCTCTATCACCCCTAACAGCCTAGTGAACC TCCTCCAAGAAACTAAAAGAATATCCTTACCTACTTGTGCCTCTCAGTTGCATTGCT TTATCATGTTTGTGGTTTGTGACATGTATGTGCTCTCAGCCATGGCATATGACAGGT ATGTGGCCATCTGCAACCCTTTACTCTATAGTATCATCATGAACAGAAGGGTCTGTA TTCAAATGGTGGTAAGTACATATTTGTATGGCTTTTCTGTGAGACTCCTACAGGCAA TTCTTACATTCCACTTGTCTTTCCGAGATTCAAATATAATAAATTCCTATTGTGA TGATGTTCCCCTAGCATGTCTACCCTATCATCATAAAAACCATTACAAAGATGTAAAAGA ACTGATATTGTTCACACTTGCTGGTTCAATACACTTTTCTCCCCTTCTTATCATCCTC ATCTCCTACACATATCAGTACTGTCTGCGCCATTGCTGAGAATTAATTCAGCTGAAAGTAGA CAAAAGGCATTTCTACTTGTGACTCGCCACCTGACTTCTATCATCATATTTTATGGT ATAATTACCTTCATGTATGCAGGGAAAAACAAATAAATTCCTGGATACAGACAA AATAGCTTCTGTTTTCTGTATTGTGAAGATGCTTTGAAGATGATTATGGAAAAATCTATGTCTTACTACAAGAT AAATGACCTTGG	MVRNTSTHISWPKPIIQKLL NSSSWDSQTIQSSKPFFRGIF LVINLSSVMGSLGLIMLIHIS PQLHTAMYFFLSHVAFVYF CYTSSITPNSLVNLLQETKRI SLPTCASQLHCFIMFVVCD MYVLSAMAYDRYVAICNPL LYSIIMNRRVCIQMVVSTYL YGFSVRLLQAILTFHLSFRD SNIINNSYCDDVPLACLPYH KNHYKDVKELILFTLAGFN TLFSLLILISYISVLSAILRIN SAESRQKAFSTCDSHLTSIIIF YGIITFMYMQGKTNNSLDT DKIASVFCIVKIPSIYSLRNH EVKDALKMIMENLCLTTR

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002512_A	39/40	GATAAATGGCTGAAGTTAAATATCATTTATGTCACTGTATTCATTCTGAAAGGAATTA CCAACCGGCCAGAGCTTCAGGCCCCGTGCTTTGGGGTGTTTTAGTTATCTATCTGG TCACAGTGCTGGCAATCTTGGGTTGATTACTTTAATCAAGATTGATACTCGACTCC ACACACCTATGTACTATTCCTCAGCCACCTGGCCTTTGTTGACCTTTACTCCTC TGCTATTACACCGAAGATGATGGTGAATTTTGTTGTGGAACGCAACACCATTCCTTT CCATGCTTGTGCAACCAACTGGGTTGTTTCTCACCTTCATGATCACTGAGTGTTT CCTTCTAGCCTCCATGGCCTACGATTGCTATGTCGCCATCTGTAGTCCCCTGCATTA TTCAACACTGATGTCAAGAAGAGTCTGCATTCAACTGGTGGCAGTTCCATATATATA CAGCTTCCTGGTTGCCCTCTTCCACACCGTTATCACTTTCCGTCGACTTACTGTGGC CCAAACTTAATTAACCATTTCTATTGTGATGACCTCCCCTTCTTAGCTCTGTCCTGCT CAGACACACACATGAAGGAAATTCTGATATTTGCCTTTGCTGGCTTTGATATGATCT CTTCCTCTCCATTGTCCTCACCTCCTACATCTTTATTATTGCCGCTATCCTAAGGAT CCGCTCTACTCAGGGCAACACAAAGCCATTCCACCTGTGGCTCCCATATGGTGAC TGTCACTATTTTCTATGGCACACTGATCTTTATGTACCTACAGCCCAAATCAAATCA CTCCTTGGACAGACAAGATGGCTTCGTATTTTACACAGTGGTGATCCCCATGTT AAACCCCCTAATCTATAGTCTAAGGAACAAAGAAGTGAAAGATGCCTCAAAGAAAG CCTTGGATAAAGGTTGTGAAAACTTACAGATATTAACATTTTTAAAAATAAGAAAA CTTTATTAAACAAGCAGCAGGAAATAAATCAAACTTTTCTT	MAEVNIIYVTVFILKGITNRP ELQAPCFGVFLVIYLVTVLG NLGLITLIKIDTRLHTPMYY FLSHLAFVDLCYSSAITPKM MVNFVVERNTIPFHACATQ LGCFLTFMITECFLLASMAY DCYVAICSPLHYSTLMSRRV CIQLVAVPYIYSFLVALFHT VITFRLTYCGPNLINHFYCD DLPFLALSCSDTHMKEILIFA FAGFDMISSSSIVLTSYIFIIA AILRIRSTQGQHKAISTCGSH MVTVTIFYGTLIFMYLQPKS NHSLDTDKMASVFYTVVIP MLNPLIYSLRNKEVKDASK KALDKGCENLQILTFLKIRK LY

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC073647_A	41/42	AACTAAAATGTTGATGAATTACTCTAGTGCCACTGAATTTTATCTCCTTGGCTTCCCT GGCTCTGAAGAACTACATCATCATATCCTTTTTGCTATATTCTTTTTTCTACTTGGTGA CATTAATGGGAAACACAGTCATCATCATGATTGTCTGTGTGGATAAACGTCTGCAGT CCCCCATGTATTTCTTCCTCGGCCACCTCTCTGCCCTGGAGATCCTGGTCACAACCA TAATCGTCCCCGTGATGCTTTGGGGATTGCTGCTCCCTGGAGTGCAGACAATATATT TGTCTGCCTGTGTTGTCCAGCTCTTCTTGTACCTTGCTGTGGGGACAACAGAGTTCG CATTACTTGGAGCAATGGCTGTGGACCGTTATGTGGCTGTCTGTAACCCTCTGAGGT ACAACATCATTATGAACAGACACACCTGCAACTTTGTGGTTCTTGTGTCATGGGTGT TTGGGTTTCTTTTTCAAATCTGGCCGGTCTATGTCATGTTTCAGCTTACTTACTGCAA ATCAAATGTGGTGAACAATTTTTTTGTGACCGAGGGCAATTGCTCAAACTATCCTG CAATAATACTCTTTTCACGGAGTTTATCCTCTTCTTAATGGCTGTTTTTGTTCTCTTT GGTTCTTTGATCCCTACACAATTGTCTCCAACGCCTACATCATCTCCACCATTCTCAAG ATCCCGTCATCCTCTGGCCGGAGGAAAATCCTTCTCCACTTGTGCCTCCCACTTCACC TGTGTTGTGATTGGCTACGGCAGCTGCTTGTTTCTCTACGTGAAACCCAAGCAAACG CAGGCAGCTGATTACAATTGGGTAGTTTCCCTGATGGTTTCAGTAGTAGTAACTCCTTTC CTCAATCCTTTCATCTTCACCCTCCGGAATGATAAAGTCATAGAGGCCCTTCGGATG GGGTGAAACGCTGCT	MLMNYSSATEFYLLGFPGS EELHHILFAIFFFYLVTLMG NTVIMIVCVDKRLQSPMYF FLGHLSALEILVTTIIVPVML WGLLLPGMQTIYLSACVVQ LFLYLAVGTTEFALLGAMA VDRYVAVCNPLRYNIIMNR HTCNFVVLVSWVFGFLFQI WPVYVMFQLTYCKSNVVN NFFCDRGQLLKLSCNNTLFT EFILFLMAVFVLFGSLIPTIV SNAYIISTILKIPSSSGRRKSF STCASHFTCVVIGYGSCLFL YVKPKQTQAADYNWVVSL MVSVVTPFLNPFIFTLRNDK VIEALRMG

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC027522_A	43/44	TTCAATGGTTCTCTGTCTCTCTATCTCTCTGTTTCTGCCTCCTCCGTCTCTTTGTTTCT CTTGCATGCAGGGCCCCATACTGTGGATCATGGCAAATCTGAGCCAGCCCTCCGAA TTTGTCCTCTTGGGCTTCTCCCTCCTTGGTGAGCTGCAGGCCCCTTCTGTATGGCCCCT TCCTCATGCTTTATCTTCTCGCCTTCATGGGAAACACCATCATCATAGTTATGGTCA TAGCTGACACCCACTACATACACCCATGTACTTCTTCCTGGGCAATTTTTCCCTGC TGGAGATCTTGGTAACCATGACTGACGCAGTGCCCAGGATGCTCTCAGACCTGTTGGTCC CCCACAAAGTCATTACCTTCACTGGCTGCATGGTCCAGTTCTACTTCCACTTTTCCCT GGGGTCCACCTCCTTCCTCATCCTGACAGACATGGCCCTTGATCGCTTTGTGGCCAT CTGCCACCACTGCGCTATGGCACTCTGATGAGCCGGGCTATGTGTGTCCAGCTGGC TGGGGCTGCCTGGGCAGCTCCTTTCCTAGCCATGTACCCACTGTCCTCTCCCGAGC TCATCTTGATTACTGCCATGGCCATGGCCATCAACCACTTCTTCTGTGACAATGAACC TCTCCTGCAGTTGTCATGCTCTGACACTCGCCTGTTGGAATTCTGGGACTTTCTGAT GGCCTTGACCTTTGTCCTGCGGGATCCCTTCCTGGTGACCCTCATCCTCATGGCTACATA GTGACCACTGTGCTGCGGATCCCCTCCTGCCAGCAGTGCCAGAAGGCTTTCTCCACT TGCGGGTCTCACCTCACACTGGTCTTCATCGGTCTTCATGCTGCAAGTCAGTAGTACCATCTTTCTGTAT GTCAGGCCTGGCAAAGCTCACTGTGTGCAAGTCAGGAAGGTCGCTGGCCTTGGTGAC TTCAGTTCTCACCCCCTTTCTCAATCCCTTTATCCTTACCTTCTGCAATCAGACAGTT AAAACAGTGCTACAGGGGCAGATGCAGAGGGGAACCTGGCCTGCCTGCCTCCATTGAGCA GATGAGCCCAGGGCCCAGGGAACCTGGCCTGCCTGCCTCCATTGAGCA	MVLCLYLSVSASPSVFCFSC MQGPILWIMANLSQPSEFVL LGFSSFGELQALLYGPFLML YLLAFMGNTIIVMVIADTH LHTPMYFFLGNFSLLEILVT MTAVPRMLSDLLVPHKVIT FTGCMVQFYFHFSLGSTSFL ILTDMALDRFVAICHPLRYG TLMSRAMCVQLAGAAWAA PFLAMVPTVLSRAHLDYCH GDVINHFFCDNEPLLQLSCS DTRLLEFWDFLMALTFVLS SFLVTLISYGYIVTTVLRIPS ASSCQKAFSTCGSHLTLVFI GYSSTIFLYVRPGKAHSVQV RKVVALVTSVLTPFLNPFIL TFCNQTVKTVLQGQMQRL KGLCKAQ

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC036216_C	45/46	TTTTGTTTTCTTCTTGCATGCAGGGCCCCATACTGTGGATCATGGCAAATCTGAGCCAG CCCTCCGAATTTGTCCTCTTGGGCTTCTCCTCCTTGGTGAGCTGCAGGCCCTTCTGT ATGGCCCCTTCCTCATGCTTTATCTTCTCGCCTTCATGGGAAAACACCATCATCATAG TTATGGTCATAGCTGACACCACCACTACATACACCCATGTACTTCTTCCTGGGCAATT TTTCCCTGCTGGAGATCTTGGTAACCATGACTGCAGTGCCCCAGGATGCTCTCAGACC TGTTGGTCCCCCACAAAGTCATTACCTTCACTGGCTGCATGGTCCAGTTCTACTTCC ACTTTTCCCTGGGGTCCACCTCCTTCCTCATCCTGACACAGACATGGCCCTTGATCGCT TTGTGGCCATCTGCCACCCACTGCCTGGGCTATGAGCCGGCTATGTGTG TCCAGCTGGCTGGGGCTGCCTGGGCAGCTCCTTTCCTAGCCATGGTACCCACTGTCC TCTCCGAGCTCATCTTGATTACTGCCATGGCCATGCTGTCGACGTCATCAACCACTTCTTCTGTG ACAATGAACCTCCTGCAGTTGTCATGCTCTGACACTGCCTGTTGGAATTCTGGG ACTTTCTGATGGCCTTGACCTTGTCCTCCAGCTCCTTGGTGACCCTCATCCTCCTA TGGCTACATAGTGACCACTGTGCTGCGGATCCCCTGCCAGCAGCTGCCAGAAGG CTTTTCCACTTGCGCGGGTCTCACCTCACCACTGGTCTTCATGGGCTACAGTAGTACCA TCTTTTCTGTATGTCAGGCCTGGCAAGTCACTCTGTGCAAGTCAGGAAGGTCGTGG CCTTGGTGACTTCAGTTCTCACCCCTTTCTCAATCCCTTTATCCTTACCTTCTGCAA TCAGACAGTTAAAACAGTGCTACAGGGGCAGATGCAGAGGCTGAAAGGCCTTTGCA AGGCACAATGATGAGCCCAGGGCCCAGGGGAACCTGGCCTGCCTCCATTGAGCA	MQGPILWIMANLSQPSEFVL LGFSSFGELQALLYGPFLML YLLAFMGNTIIIVMVIADTH LHTPMYFFLGNFSLLEILVT MTAVPRMLSDLLVPHKVIT FTGCMVQFYFHFSLGSTSFL ILTDMALDRFVAICHPLRYG TLMSRAMCVQLAGAAWAA PFLAMVPTVLSRAHLDYCH GDVINHFFCDNEPLLQLSCS DTRLLEFWDFLMALTFVLS SFLVTLISYGYIVTVLRIPS ASSCQKAFSTCGSHLTLVFI GYSSTIFLYVRPGKAHSVQV RKVVALVTSVLTPFLNPFIL TFCNQTVKTVLQGQMQRL KGLCKAQ

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC036216_B	47/48	AATGGCAGAAACTCTACAACTCAATTCCACCTTCCTACACCCAAACTTCTTCATACT GACTGGCTTTCCAGGGCTAGGAAGTGCCCAGACTTGGCTGACACTGGTCTTTGGGC CCATTTATCTGCTGGCCCCTGCTGGCAATGGAGCACTGCCGGCAGTGGTGTGGATA GACTCCACACTGCACCAGCCCATGTTTCTACTGTTGGCCATCCTGGCAGCCACAGAC CTGGGCTTAGCCACCATCTATAGCCCCAGGGTTGCTGCTGTGCTGTGGCTGGGCCCC CGATCTGTGCCATATGCTGTGTGCCTGGTCCAGATGTTCTTTGTACATGCACTGACT GCCATGGAATCAGGTGTGCTTTTGGCCATGGCCTGTGATCGTGCTGCGGCAATAGG GCGTCCACTGCACTACCCTGTCCTGGTCACCAAAGCCTGTTGTGGGTTATGCAGCCTT GGCCCTGGCACTGAAAGCTGTGGGTAACACAGCCACCAACTATATGGTCTGGCACTT GTTTGAGCACTTCCAAGCCAAGACCATAGGCCATACCTATTGTGCACACATGGCAG TGGTAGAACTGGTGGTGGGTAACACAGGCCACCAACTTATATGGTCTGGCACTT TCACTGGCCATCTCAGGTATGGATATTCTGGGTATCACTGGCTCCTATGGACTCATT GCCCATGCTGTGCTGCAGCTACCTACCCGGGAGGCCATGCCAAGGCCTTTGGTAC ATGTAGTTCTCACATCTGTGTCATCACACTGTGCCACCTGCCCTCAACCCCCTCATCTAC CTCGCACACCGCTTTGGTCATCACACTGTGCCACCTGCCCTCAACCCCCTCATCTATGGGGCCCGCACC AACATCTACTTGCTGCTGCCACCTGCCCTCAACCCCCTCATCTATGGGGCCCGCACC AAGCAGATCAGAGACCGACTCCTGGAAACCTTCACATTCAGAAAAAAGCCCGTTGTA AT	MAETLQLNSTFLHPNFFILT GFPGLGSAQTWLTLVFGPIY LLALLGNGALPAVVWIDST LHQPMFLLLAILAATDLGLA TSIAPGLLAVLWLGPRSVPY AVCLVQMFFVHALTAMESG VLLAMACDRAAAIGRPLHY PVLVTKACVGYAALALALK AVAIVVPFPLLVAKFEHFQA KTIGHTYCAHMAVVELVVG NTQATNLYGLALSLAISGM DILGITGSYGLIAHAVLQLPT REAHAKAFGTCSSHICVILA FYIPGLFSYLAHRFGHHTVP KPVHILLSNIYLLLPPALNPL IYGARTKQIRDRLLETTFFR KSPL

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC036216_A	49/50	TGCATCATGAGTCACACCAATGTTACCATCTTCCATCCTGCAGTTTTTGTCCTTCCTG GCATCCCTGGGTTGGAGGCTTATCACATTTGGCTGTCAATACCTCTTTGCCTCATT ACATCACTGCAGTCCTGGGAAACAGCATCCTGATAGTGGTTATTGTCATGGAACGT AACCTTCATGTGCCCATGTATTTCTTCCTCTCAATGCTGGCCGTCATGGACATCCTG CTGTCTACCACCACTGTGCCCAAGGCCCTAGCCATCTTTGGCTTCAAGCACACATAAC ATTGCTTTTGATGCCTGTGTCACCCAAGGCTTCTTTGTCCATATGATGTTTGTGGGG GAGTCAGCTATCCTGTTAGCCATGGCCTTTGATCGCTTTGTGGCCCATTTGTGCCCCA CTGAGATATACAACAGTGCTAACATGGCCTGTTGTGGGGAGGATTGCTCTGGCCGT CATCACCCGGAAGCTTCTGCATCATCTTCCCAGTCATATTCTTGCTGAAGCGGCTGCC CTTCTGCCTAACCAACATTGTTCCTCCTACTGTGAGCATATTGGAGTGGCTCG TTTAGCCTGTGTCGACATCACTGTTAACATTTGGTATGGCTTCTCAGTGCCCATTGT CATGGTCATCTTGGATGTTATCCTCATCGCTGTGTCTTACTCACTGATCCTCCGAGC AGTGTTTCGTTTGCCCTCCCAGGATGCTCGGCACAAGGCCCTCAGCACTTGTGGCTC CCACCTCTGTGTCGTTTATGTTTTATGTTCCATCCTTCTTTACCTTATGACCCAT CATTTTGGGCGGTAATATTCCTCAACATGTCCATGTCCATATCTTGCTGGCCAATCTTTATGTG GCAGTGCCACCAATGCTGAACCCCATTGTCTATGGTGTGAAGACTAAGCAGATACG TGAGGGTGTAGCCCACCGGTTCTTTGACATCAAGACTTGGTGCTGTACCTCCCTCT GGGCTCATGAATCTTCAT	MSHTNVTIFHPAVFVLPGIP GLEAYHIWLSIPLCLIYITAV LGNSILIVVIVMERNLHVPM YFFLSMLAVMDILLSTTTVP KALAIFWLQAHNIAFDACV TQGFFVHMMFVGESAILLA MAFDRFVAICAPLRYTTVLT WPVVGRIALAVITRSFCIIFP VIFLLKRLPFCLTNIVPHSYC EHIGVARLACADITVNIWY GFSVPIVMVILDVILIAVSYS LILRAVFRLPSQDARHKALS TCGSHLCVILMFYVPSFFTL LTHIHFGRNIPQHVHILLANL YVAVPPMLNPIVYGVKTKQ IREGVAHRFFDIKTWCCTSP LGS

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC026090_C	51/52	ACTTATCATGCTAACACTGAATAAAACAGACCTAATACCAGCTTCATTTATTCTGAA TGGAGTCCCAGGACTGGAAGACACACAACTCTGGATTTCCTTCCCATTCTGCTCTAT GTATGTTGTGGCTATGGTAGGGAATTGTGGACTCCTCTACCTCATTCACTATGAGGA TGCCCTGCACAAACCCATGTACTACTTCTTTGGCCATGCTTTCCTTACTGACCTTGTT ATGTGCTCTAGTACAATCCCTAAAGCCCTGCATCTTCTCGGTTTCATCTCAAGGAC ATTGGATTTGATGAATGCCTTGTCCAGATGTTCTTCATCCACACCTTCACAGGGATG GAGTCTGGGGTGCTTATGCTTATGGCCCCTGGATCGCTATGTGGCCATCTGCTACCCC TTACGCTATTCAACTATCCTCACCAATCCTGTAATTGCAAAGGTTGGGACTGCCACC TTCCTGAGAGGGTATTACTTCATTATTCCCTTACTTCCTGACCACACTGTCTGCCCCT ACTGCCAGAGCAATATACTTCCCATACCTACTGTGACCACATGTCTGTAGCCAAAT TGTCCTGTGGTAAGTCAAGGTCAATGCCATCTATGGTCTGATGGTTGCCCTCCTGA TTGGGGGCTTTGACATACTGTGTATCACCATCTCCTATACCATGATTCTCCGGGCAG TGGTCAGCCTCTCCTCAGCAGATGCTCGGCAGAAGGCCTTTAATACCTGCACTGCCC ACATTTGTGCCATTGTTTTCTCCTATACTCCAGCTTTCTTCTCCTCTTTTCCCACCG CTTTGGGAACACATAATCCCCCCCTTCTTGCCACATCATTGTAGCCAATATTTATCT GCTCCTACCACCCACTATGAACCCTATTGTCTATGGGGTGAAAAACCAAACAGATAC GAGACTGTGTCATAAGGATCCTTCAGGTTCTCAAGGATACCAAATCCTACAGCATGT GAATGAACACTTGCCAGGA	MLTLNKTDLIPASFILNGVP GLEDTQLWISFPFCSMYVV AMVGNCGLLYLIHYEDALH KPMYYFLAMLSFTDLVMCS STIPKALCIFWFHLKDIGFDE CLVQMFFIHTFTGMESGVL MLMALDRYVAICYPLRYST ILTNPVIAKVGTATFLRGVL LIIPFTFLTKRLPYCRGNILP HTYCDHMSVAKLSCGNVK VNAIYGLMVALLIGGFDILC ITISYTMILRAVVSLSSADAR QKAFNTCTAHICAIVFSYTP AFFSFFSHRFGEHIIPPSCHII VANIYLLLPPTMNPIVYGVK TKQIRDCVIRILSGSKDTKSY SM

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC026090_B	53/54	AATTCATGTTGAATCATGAATCATGTCTGCATCTCTCAAAATCTCCAATAGCTCC AAATTCCAGTCTCTGAGTTCATCTCGTGGGATTCCCGGGCATTCACAGCTGGCAA CACTGGCTATCTCTGCCCCTGGCACTACTGTATCTCTCAGCACTTGCTGCAAACACC CTCATCCTCATCATCATCTGGCAGAGAACCCTTCTTTACAGCAGCCATGTATATTTCC TTGGCATCCTCTGTATGGTAGACACATGGGTCTGGCCACTACTATCATCCCTAAGATCC TGGCCATCTTCTGGTTTGATGCCAAGGTTATTAGCCTCCCTGAGTGCTTTGCTCAGA TTTATGCCATTCACTTCTTTGTGGGCATGGAGTCTGGTATCCTACTCTGCATGGCTTT TGATAGATATGTGGCTATTTGTCACCCTCTTCGCTATCCATCAATTGTCACCAGTTC CTTAATCTTAAAAGCTACCCTGTTCATGGTGCTGAGAAATGGCTTATTTGTCACTCC AGTGCCTGTGCTTGCAGCACAGCGTGATTATTGCTCCAAGAATGAAATTGAACACT GCCTGTGCTCTAACCTTGGGGTCACAAGCCTGGCTTGTGACGAGGCCAAAC AGCATTTGCCAGTTGGTTCTGGCATGGCTTGGAATGGGGAGTGATCTAAGTCTTATT ATACTGTCATATATTTTGATTCTGTACTCTGTACTTAGACTGAACTCAGCTGAAGCT GCAGCCAAGGCCCTGAGCACTTGTAGTTCACATCTCACCCTCATCCTTTTCTTTTAC ACTATTGTTGTAGTGATTTCAGTGACTCATCTCATCTGACAGAGATGAAGGCTACTTTGATT CCAGTTCTACTTAATGTGTTGCACAACATCATCCCCCTACCCTTCCCTACAGTTT ATGCACTTCAGACCAAAGAACTTAGGGCAGCCTTCCAAAAGGTGCTGTTTGCCCTTAS CAAAAGAAATAAGATCTTAGAGACCTTCTCCATGAT	MNHMSASLKISNSSKFQVSE FILLGFPGIHSWQHWLSLPL ALLYLSALAANTLILIIWQN PSLQQPMYIFLGILCMVDM GLATTIIPKILAIFWFDAKVI SLPECFAQIYAIHFFVGMES GILLCMAFDRYVAICHPLRY PSIVTSSLILKATLFMVLRNG LFVTPVPVLAAQRDYCSKN EIEHCLCSNLGVTSLACDDR RPNSICQLVLAWLGMGSDL SLIILSYILILYSVLRLNSAEA AAKALSTCSSHLTLILFFYTI VVVISVTHLTEMKATLIPVL LNVLHNIIPPSLNPTVYALQ TKELRAAFQKVLFALTKEIR S

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC026090_A	55/56	TTTATCCTGATGGGATTCCCTGGCATTCACAGTTGGCAGCACTGGCTCTCCCTGCCC CTGGCTCTGCTCTACCTCTTAGCTCTCAGTGCCAACATCCTTATCCTGATCATCATCA ACAAAGAGGCAGCACTGCACCAGCCTATGTACTATTTCCTGGCATCTTGGCTATG GCAGACATAGGCCTGGCTACCACCATCAGTCTCCTGGAGTGCTTTGCTCAGATGTATGCCATACATTGC AATGCTAAGACCATCAGTCTCCTGGAGTGCTTTGCTCAGATGTATGCCATACATTGC TTTGTGGCCATGGAATCAAGTACCTTTGTCTGCATGGCTATTGATAGATATGTAGCC ATTTGTCGACCGCTACGATATCCATCAATCACTGAATCTTTGTTTTCAAAGCA AATGGGTTCATGGCACTGAGAAACAGCCTGTGTCTCATCTCAGTGCCTCTGTTGGCT GCCCAGAGGCATTACTGCTCCCAGAATCAAATTGAGCACTGTCTTTGTTCTAACCTT GGAGTCACTAGCCTATCTTGTGATGATCGAAGAATCAATAGCATTAACCAGGTCCTT TTGGCTTGGACACTCATGGGAGTGACCTGGTTTGATTATTTATCATATGCTCTA ATACTTTACTCTGTCCTGAAGCTGAACTCTCCAGAAGCTGCATCCAAGGCCTTAAGT ACCTGCACCTCCCACCTCATCTTAATCCTTTTCTTCTACACAGTCATCATTGTGATTT CCATTACTCGTAGTACAGGAATGAGAGTTCCCCTTATTCCAGTTCTACTTAATGTGC TACACAATGTCATTCCCCGCCCTGAACCCCATGGTATATGCACTCAAGAACAAGG AACTCAGGCAAGGCTTATACAAGGTACTTAGACTGGGAGTGGAAGGGCACCTGATAT GGAAAAGATATTTCATTTTTGAAAATTTTCTTCACAT	MGFPGIHSWQHWLSLPLAL LYLLALSANILILIINKEAAL HQPMYYFLGILAMADIGLA TTIMPKILAILWFNAKTISLL ECFAQMYAIHCFVAMESST FVCMAIDRYVAICRPLRYPS IITESFVFKANGFMALRNSL CLISVPLLAAQRHYCSQNQI EHCLCSNLGVTSLSCDDRRI NSINQVLLAWTLMGSDLGL IILSYALILYSVLKLNSPEAA SKALSTCTSHLJLILFFYTVII VISITRSTGMRVPLIPVLLNV LHNVIPPALNPMVYALKNK ELRQGLYKVLRLGVKGT

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002358_A	57/58	CCAATGACTGGGGGAGGAAATATTACAGAAATCACCTATTTCATCCTGCTGGGATT CTCAGATTTTCCCAGGATCATAAAAGTGCTCTTCACTATATTCCTGGTGATCTACAT TACATCTCTGGCCTGGAACCTCTCCCTCATTGTTTAATAAGGATGGATTCCCACCT CCATACACCCATGTATTTCTTCCTCAGTAACCTGTCCTTCATAGATGTCTGCTATATC AGCTCCACAGTCCCCAAGATGCTCTCCAACCTCTTACAGGAACAGCAAACTATCACT TTTGTTGGTTGTATTATTCAGTACTTTATCTTTTCAAGCGATGGGACTGAGTGAGTCT TGTCTCATGACAGCCATGGCTTATGATCGTTATGCTGCCATTTGTAACCCCCTGCTC TATTCATCCATCATGTCACCCACCCTCGTGTTGTTGGATGGTACTGGGAGCCTACATG ACTGGCCTCACTGCTTCTTATTCCAAATTGGTGCTTTGCTTGCTTCAACTCCACTTCTGTG GGTCTAATGTCATCAGACATTTCTTCTGTGACATGCCCCAACTGTTAATCTTGTCCT GTACTGACACTTCTTTGTACAGGTCATGACTGCTATATTAACCATGTTCTTTTGGGA TAGCAAGTGCCCTAGTTATCATGATATCCTATGGCTATATTGGCATCCATCATGA AGATCACTTCAGCTAAAGGCAGTCCAAAGGCATTCAACACCTGTCCTTCTCATCTAA CAGCTGTTTCCCTCTTCTATACATCAGGAATCTTTGTCTATTTGAGGTCCAGCTCTG GAGGTTCTTCAAGCTTTGACAGATTTGCATCTGTTTTCTACACTGTGGTCATTCCCA TGTTAAATCCCTGATTTACAGTTGAGGAACAAAGAAATTAAAGATGCCTTAAAG AGGTTGCAAAGAGAGAAAGTGCTGCTGA	MTGGGNITEITYFILLGFSDF PRIIKVLFTIFLVIYITSLAWN LSLIVLIRMDSHLHTPMYFF LSNLSFIDVCYISSTVPKMLS NLLQEQQTITFVGCIIQYFIF STMGLSESCLMTAMAYDR YAAICNPLLYSSIMSPTLCV WMVLGAYMTGLTASLFQIG ALLQLHFCGSNVIRHFFCDM PQLLILSCTDTFFVQVMTAI LTMFFGIASALVIMISYGYIG ISIMKITSAKGSPKAFNTCAS HLTAVSLFYTSGIFVYLRSSS GGSSSFDRFASVFYTVVIPM LNPLIYSLRNKEIKDALKRL QKRKCC

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002517_C	59/60	ACTTATGAAAGAGGTTCGAGGCAGAAATCAAACAGAAGTAACAGAATTTCTCCTCT TAGGACTTTCCGACAATCCAGATCTACAAGGAGTCCTCTTTGCATTGTTTCTGTTGA TCTATATGGCAAACATGGTGGGCAATTTGGGGATGATTGTATTGATTAAGATTGAT CTCTGTCTCCACACCCCATGTATTTCTTTCTCAGTAGCCTCTCTTTTGTAGATGCCT CTTACTCTTCTTCCGTCACTCCCAAGATGCTGGTGAACCTCATGGCTGAGAATAAGG CCATTTCTTTTCATGGATGTGCTGCCCCAGTTCTACTTCTTTGGCTCCTTCCTGGGGAC TGAGTGCTTCCTGTTGGCCATGATGGCATATGACCGGCTATGCAGCCATTTGGAACCC CCTGCTCTACCCAGTTCTCGTGTCTGGGAGAATTTGCTTTTTGCTAATAGCTACCTC CTTCTTAGCAGGTTGTGGAAATGCAGCCATACATACAGGGATGACTTTAGGTTGTC CTTTTGTGGTTCTAATAGGATCAACACCATTTCTACTGTGACACCCCGCCACTGCTCAA ACTCTCTGCTCTGATACCCACTTCAATGGCATTGTGATCATGGCATTCTCAAGTTTT ATTGTCATCAGCTGTGTTATGATTGTCCTCACCTGTATCTTCATTGCCG TCTTGAAGATGCCTTCGTTAGAGGGCAGGCACAAAGCCTTCTCCACCTGTGCCTCTT ACCTCATGGCTGTCACCATATTCTTTGGAACAATCCTCTTCATGTACTTGCGCCCTA CATCTAGCTACTCAATGGAGCAAGACAAGGTTGTCTCTGTCTTTTATACAGTAATAA TCCCTGTGCTAAATCCCCTCCTCATCTATAGTTTAAAAAATAAGGATGTAAAAAGGCCC TAAAGAAGATCTTATGGAAACACATCTTGTAGAGCCAT	MKEVRGRNQTEVTEFLLLG LSDNPDLQGVLFALFLLIYM ANMVGNLGMIVLIKIDLCL HTPMYFFLSSLSFVDASYSS SVTPKMLVNLMAENKAISF HGCAAQFYFFGSFLGTECFL LAMMAYDRYAAIWNPLLY PVLVSGRICFLLIATSFLAGC GNAAIHTGMTFRLSFCGSN RINHFYCDTPPLLKLSCSDT HFNGIVIMAFSSFIVISCVMI VLISYLCIFIAVLKMPSLEGR HKAFSTCASYLMAVTIFFGT ILFMYLRPTSSYSMEQDKV VSVFYTVIIPVLNPLIYSLKN KDVKKALKKILWKHIL

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002517_B	61/62	GAAATGTCCAACACACAAATGGCAGTGCAATCACAGAATTCATTTACTTGGGCTCAC AGATTGCCCGGAACTCCAGTCTCTGCTTTTTGTGCTGTTTCTCGGTTGTTTACCTCGTC ACCCTGCTAGGCAACCTGGCATGAATAATGTTAATGAGACTGGACTCTCGCCTTCAC ACGCCCATGTACTTCTTCCTCACTAACTTAGCCTTTGTGGATTTGTGCTATACATCA AATGCAACCCCGCAGATGTCGACTAATATCGTATCTGAGAAGACCATTTCCTTTGCT GGTTGCTTTACACAGTGCTACACATTTTCATTGCCCTTCTACTCACTGAGTTTTACATGC TGGCAGCAATGGCCTATGACCGGCTATGTGGCCATATATGACCCCTCTGCGCTACAGTG TGAAAACGTCCAGGAGAGTTTGCATCTGCTTGGCCACATTTCCCTATGTCTATGGCT TCTCAGATGGACTCTTCCAGGCCATCCTCGACCTTCCGCCTGACCTTCTGTAGATCCA GTGTCATCAACCACTTCTACTGTCGCTGACCCGCCGCTCATTAAGCTTTCTTGTTCTG ATACTTATGTCAAAGAGCATGCCATGTTCATATCTGCTTCATTCTTGCTGCCATCCTCCGGATCAA CCCTCACCATCGTCTTGGTGTCCTATGCCTTCATTCTTGCTGCTGCCATCCTCCGGATCAA ATCAGCAGAGGGAAGGCACAAGGCATTCTCCACCTGTGGTTCCCATATGATGGCTG TCACCCTGTTTTATGGGGACTCTCTTTGCATGTATATAAGACCAACAGATAAGA CTGTTGAGGAATCTAAAAATAATAGCTGTCTTTTACACCTTTGTGAGTCCGGTACTTA ATCCATTGATCTACAGTCTGAGGAATAAAAGATGTGAAGCAGGCCTTGAAGAATGTC CTGAGATGAAATATTGTCATGACCCATGGTGATGCCTTTGTTCCTAATAAACATTAA ATCGAAATCTTTGGCTCACAT	MSNTNGSAITEFILLGLTDC PELQSLLFVLFLVVYLVTLL GNLGMIMLMRLDSRLHTPM YFFLTNLAFVDLCYTSNATP QMSTNIVSEKTISFAGCFTQ CYIFIALLLTEFYMLAAMAY DRYVAIYDPLRYSVKTSRR VCICLATFPYVYGFSDGLFQ AILTFRLTFCRSSVINHFYCA DPPLIKLSCSDTYVKEHAMF ISAGFNLSSSLTIVLVSYAFIL AAILRIKSAEGRHKAFSTCG SHMMAVTLFYGTLFCMYIR PPTDKTVEESKIIAVFYTFVS PVLNPLIYSLRNKDVKQAL KNVLR

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Table 1

Acc. No.	SEQ ID NO (Nucl)/ SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP0002418_E	63/64	CCATGCAGAGGAGCAATCACACAGTGACTGAGTTTATACTGCTGGGCTTCACCACA GACCCAGGGGATGCAGCTGGGCCTCTTCGTGGTGTTCCTGGGCGTGTACTCTCTCACT GTGGTAGGAAATAGCACCCTCATCGTGTTGATCTGTAATGACTCCCACCTCCACACA CCCATGTATTTTGTCGTTGGAAATCTGTCGTTTCTGGATCTCTGGTATTCTTCTGTCT ACACCCCAAAGATCCTCAGTAGTCTGCATCTCTGAAGACAAAAGCATCTCCTTTGCTG GCTGCCTGTCGTCAGTTCTTCTTCTCTGCAGGCGTGGCCTATAGTGAGTGCTGCTTAC TGGCTGCCATGGCTTATGACCGCTACGTGGCCATCTCCAAGCCCCTGCTTTATGCCC AGGCCATGTCCATAAAGCTGTGTGCATTGCTGCTAGCAGTCTCATATTGTGGTGGCT TTATTAACTCTTCAATCATCACCAAGAAAACGTTTTCCTTTAACTTCTGCCGTGAAA ACATCATTGATGACTTTTTCTGTGATTTGCTTCCCTTGGTGGAGCTGGCCTGTGGCG AGAAGGGCGGCTATAAAATTATGATGTACTTCCTGCTGGCCTCCAATGTCATCTGCC CCGCAGTGCTCATCCTGGCCTCATCCTTTATCATCACCAGTGTCTTGAGGATCT CCTCCTCCAAGGGCTACCTCAAAGCCTTCTCCACATGCTCCTCCCACCTGACCTCTG TCACTTTATACTATGGCTCCATTCTCTACATCTACGCTCTCCCCAGATCTAGCTATTC TTTGATATGGACAAAATAGTTTCTACACTGTGGTATTCCCCATGTTGAA TCTCATGATCTACAGCCTAAGGAATAAGGATGTGAAAGAGGCTCTGAAAAAACTTC TCCCATAAATCAAGATTATCTCCACCAGAGGAGAAACAAAGACGACCTTAGATGGA	MQRSNHTVTEFILLGFTTDP GMQLGLFVVFLGVYSLTVV GNSTLIVLICNDSHLHTPMY FVVGNLSFLDLWYSSVYTP KILVICISEDKSISFAGCLCQF FFSAGLAYSECCLLAAMAY DRYVAISKPLLYAQAMSIKL CALLVAVSYCGGFINSSIITK KTFSFNFCRENIIDDFFCDLL PLVELACGEKGGYKIMMYF LLASNVICPAVLILASYLFIIT SVLRISSSKGYLKAFSTCSSH LTSVTLYYGSILYIYALPRSS YSFDMDKIVSTFYTVVFPM LNLMIYSLRNKDVKEALKK LLP

Table 1

SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
Acc. No.		
GMAP002418_B		
65/66	AATAAGTGTACTTCCAATGATATATTATTAAATGTGGTTAGCATAATAAGATTACTTTTT TTACTGTTTATCCTTTAGAGTTCACAGAAGATTGGGGTTACAGCAAGTGCTCTTT TTCATCTTTCTCATCATTTATGTCATCAGCCTCTCAGGCAACATCATTCTGAATTCTC TCATCTGTGCTGATTCTTGGCCCTACACACCCATGTATTTCTTCACTGGAAACCGGT TCCTTCTGGATCTCTGGTATTCCTCGTCCACATCCCGATATCCTGCTGACTTGCAT TTCTGATGACAAAACCATCTCCTTTCCTGGCTGCTCAGTTCTTCTCTGCTGTG TTGGCCTTAAATGAGTGCTATATGATGGCTTCCATGGCTTATGACCGCTACATGGCA ATCTCCAAGCCCTGCTTTATTCCTGGGCCACATTCCCAGAGTTATGTGCCAGTCTT GTTGAGGCTTCACACCTTGGCGGCTTTGTAAACTCAACCATCACCAGTGAGACA CCTACCTTGAGCTTCTGTGGCAGCAATATCATTGATGATTTCTTCTGTGATCTGCCC CCACTTGTAAAGTTGGTGTGTGATGTGAAGGAGCGCTACCAGGCTGTGCTGCATTTT ATGCTTGCCTCCAATCATCACTCCCACTGCACTTATTCTTGCGTCCATCTTCATCA TTGCAGCCATCTCGAAGATCCGTTCCATTAAGGGCCGCCTCCAGGTCTTCTCCACTT GTGGGTCTCCCCTGACGGCTCTCACCTTGTACTATGGTGCAATCTTCTTTATTTACTC CCAACCAAGAACTAGCTATGCCTAAAAATGGATAAATTGGGGTCAGTGTTCTATA CTGTGGTGATTCCAATGCTAAACCCCTTGATCTATAGCTTAAGAAATAAGGATGTCA AAGATGCCTTGAAGAAAATGTTAGATAGACTTCAGTTTCTTAAAGAAAAATATTGG TAAACAATTTTTAACAGATTATCTCCAC	MILLNVVSIIRLLFLLFILLEF TEDLGLQQVLFFIFLIIYVISL SGNIILNSLICADSWPYTPM YFFTGNRFLLDLWYSSVHIP DILLTCISDDKTISFPGCLAQ FFSAVLALNECYMMASMA YDRYMAISKPLLYSWATFP ELCASLVEASHLGGFVNSTII TSETPTLSFCGSNIIDDFFCD LPPLVKLVCDVKERYQAVL HFMLASNHHSHCTYSCVHL FIIAAISKIRSIKGRLQVFSTC GSPLTALTLYYGAIFFIYSQP RTSYALKMDKLGSVFYTVV IPMLNPLIYSLRNKDVKDAL KKMLDRLQFLKEKYW

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002345_C	67/68	CTACATAATTCCCAATGGAGAACAACACAGAGGTGACTGAATTCATCCTTGTGGGG TTAACTGATGACCCAGAACTGCAGATCCCACTCCTTCATCCTTTCATCTAC CTCATCACTCGGTTGGGAACCTGGGGATGATTGAATTGATTCTACTGGACTCCTGT CTCCACACCCCATGTACTTCTTCCTCAGTAACCTCTCCCTGGTGGACTTTGGTTATT CCTCAGCTGCTGCTCACTCCCAAGGTGATGGTGGGGGTTTCTCACAGGAGACAAATTCATAT TATATAATGCTTGTGCCACACAATTCTTCTTCTTTGTGTAGCCTTTATCACTGCAGAAA GTTTCCTCCTGGCATCAATGGCCTATGACCGCTATGCAGCATTGTGTAAACCCCTGC ATTACACCACCACCATGACAACAACAAATGTATGTGCTTGCCTGCCATAGGCTCCTACA TCTGTGGTTTCCTGAATGCATCCATTCATACTGGGAACACTTTCAGGCTCTCCTTCT GTAGATCCAATGTAGTTGAACACTTTTCTGTGATGCTCCTCCTCTTGACTCTCTC ATGTTCAGACAACTACATCAGTGAGATGGTTATTTTTTGTGGTGGGATTCAATGA CCTCTTTTCTATCCTGGTAATCTTGATCTCCTACTTATTTATCACCATCATG AAGATGCGCTCACCTGAAGGACGCCAGAAGGCCTTTCTACTTGTGCTTCCCACCTT ACTGCAGTTCCATCTTTATGGGACAGGAATCTTTATGTACTTACGACCTAACTCC AGCCATTCATGGCACAGACAAAATGGCATCGTGTTCTATGCCCATAGTCATTCCC ATGTTGAATCCACTGGTCTACAGCCTGAGGAACAAAGAGGTTAAGAGTGCCTTTAA AAAGACTGTAGGGAAGGCAAAGGCCTCTATAGGATTCATATTTTAATTATAAAGAA TTCACAATAAGATAATTTTTTCCACCTCACTATTAAATCTTTGTCTAC	MENNTEVTEFILVGLTDDPE LQIPLFIVFLFIYLITLVGNLG MIELILLDSCLHTPMYFFLS NLSLVDFGYSSAVTPKVMV GFLTGDKFILYNACATQFFF FVAFITAESFLLASMAYDRY AALCKPLHYTTMTTNVCA CLAIGSYICGFLNASIHTGNT FRLSFCRSNVVEHFFCDAPP LLTLSCSDNYISEMVIFFVV GFNDLFSILVILISYLFIFITIM KMRSPEGRQKAFSTCASHL TAVSIFYGTGIFMYLRPNSS HFMGTDKMASVFYAIVIPM LNPLVYSLRNKEVKSAFKK TVGKAKASIGFIF

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002345_A	69/70	ATAATACTGATGGAGAATTGTACGGAAGTGACAAAGTTCATTCTTCTAGGACTAAC CAGTGTCCCAGAACTACAGATCCCCCTCTTTATCTTGTTCACCTTCACCTCACCTCCTC ACTCTGTGTGGGAACCTGGGGATGATGTTGCTGATCCTGATGGACTCTTGTCTCCAC ACCCCCATGTACTTTTTCCTCAGTAACCTGTCTCTGGTGGACTTTGGATACTCCTCA GCTGTCACTCCCAAGGTCATGGCTGGGTTCCTTAGAGGAGACAAGGTCATCTCCTAC AATGCATGTGCTGTTCAGATGTTCTTTGTAGCCTTGGCCACGGTGGAAAATTAC TTGTTGGCCTCAATGGCCTATGACCGCTATGCAGCAGTGTGCAAACCCTACACTAC ACCACCACCATGACGGCCAGTGTAGGTGCCTGTCTGGCCCTAGGCTCATATGTCTGT GGCTTCCTAAATGCCCTCATTCCACATTGGGGGCATATTCAGTCTCTCTTTCTGTAAA TCCAATCTGGTACATCACTTTTTCTGTGATGTTCCAGCAGTCATGGCTCTGTCTTGCT CTGATAAACACCAGTGAGGTGATTCGGTTTTTATGTCAAGCTTAATATCTTTT TTGTTCTTCTAGTTATCTTTATCTCCTACTTGTTCATATTCATCACCATCTTGAAGAT GCATTCAGCTAAGGGACACCAAAAAGCATTGTCCACCTGTGCCTCTCACTTCACTGC AGTCTCCGTCTTCTTATGGGACACAGTAATCTTCATCTGTCTGTTCTATGCTATGATC CTCCATGGACAACAGACACAAATGGCATCTGTGTTCTATGCTATGATCATCCCCATGCT GAACCCTGTGGTCTACAGCCTGAGGAACAGAGAGAAGTCCAGAATGCATTCAAGAAAG TGTTGAGAAGGCAAAAATTTCTATAA	MENCTEVTKFILLGLTSVPE LQIPLFILFTFIYLLTLCGNLG MMLLILMDSCLHTPMYFFL SNLSLVDFGYSSAVTPKVM AGFLRGDKVISYNACAVQM FFFVALATVENYLLASMAY DRYAAVCKPLHYTTMTAS VGACLALGSYVCGFLNASF HIGGIFSLSFCKSNLVHHFFC DVPAVMALSCSDKHTSEVI LVFMSSFNIFFVLLVIFISYLF IFITILKMHSAKGHQKALST CASHFTAVSVFYGTVIFIYL QPSSSHSMDTDKMASVFYA MIIPMLNPVVYSLRNREVQ NAFKKVLRRQKFL

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001524_B	71/72	TGGTCCTCCTTCTCTTGTCCCCTCCTCCGACTCTCCTGCCTGACCAAAAAGAATGGCAGCC AAAAACTCTTCTGTGACAGAGTTTATCCTCGAAGGCTTAACCCACCAGCGCCGGGACT GCGGATCCCCCGCCTTCTTCCTGTTTCTGGGTTTCTACACGGTCACCGTGGTGGGGAA CCTGGGCTTGATAACCCTGATTGGGCTGAACTCTCACCTGCACACTCCCATGTACTT CTTCCTTTTTAACCTCTCTCTTTAATAGATTTCTGTTTCTCCACTACCATCACTCCCAAA ATGCTGATGAGTTTTGTCTCAAGGAAGAACATCATTTCCTTCACAGGGTGTATGACT CAGCTCTTCTTCTTCTGCGTCTTTGTCGTCTCTGAGTCCTTCATCCTGTCAGCGATGG CGTATGACCGGCTACGTGGCCATCGTAACCCACTGTTGTACACAGTCACCATGTCTT GCCAGGTGTGTTGCTCCTTTTGTTGGGTGCCTATGGGATGGGGTTTGCTGGGGCCA TGGCCCACAGGAAGCATAATGAACCTGACCTTCTGTGCTGACAACCTTGTCAATC ATTTCATGTGTGACATCCTTCCTCCTCCTTGAGCTCTCCTGCAACAGCTCTTACATGA ATGAGCTGGTGGTCTTTATTGTGGTGGCTGTTGACGTTGGAATGCCCATTGTCACTG TCTTTATTTCTTATGCCCTCATCCTCTCCAGCATTCTACACAACAGTTCTACAGAAGG CAGGTCCAAAGCCTTTAGTACTTGCAGTTCCCACATAATTGTAGTTTCTCTTTTCTTT GGTTCTGGTGCTTTCATGTATCTCAAACCCTTTCAAACCCGTGTTAAACCATTAATCTAT AAAGTGTCCCCTGTTCTATACCATATAATAGTCCCCGTGTTAAACCATTAATCTAT AGCTTGAGGAACAAGGATGTCAAAGTGCCCTGAGGAGAACTTTGGGCAGAAAAAT CTTTTCTTAAGAAAGGATTA	MAAKNSSVTEFILEGLTHQP GLRIPLFLFLGFYTVVVG NLGLITLIGLNSHLHTPMYF FLFNLSLIDFCFSTTITPKML MSFVSRKNIISFTGCMTQLF FFCFFVVSESFILSAMAYDR YVAICNPLLYTVTMSCQVC LLLLLGAYGMGFAGAMAH TGSIMNLTFCADNLVNHFM CDILPLLELSCNSSYMNELV VFIVVAVDVGMPIVTVFISY ALILSSILHNSSTEGRSKAFS TCSSHIIVVSLFFGSGAFMYL KPLSILPLEQGKVSSLFYTII VPVLNPLIYSLRNKDVKVA LRRTLGRKIFS

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001260_A	73/74	ATGACACCTGGAGAACTAGCCCTTGCCAGTGGCAACCACACCCCAGTCACCAAGTT CATCTTGCAGGGATTCTCCAATTATCCAGACCTCCAGGAGCTTCTTCGGAGCCAT CCTGCTCATCTATGCCATAACAGTGGTGGGCAACTTGGGAATGATGGCACTCATCTT CACAGACTCCCATCTCCAAAGCCCAATGTATTTCTTCCTCAATGTCCTCGTTTCTT GATATTTGTTACTCTCTCTGTGTGGTCACACCTAAGCTCTTGGTCAACTTCCTGGTCTCTG ACAAGTCCATCTCTTTTGAGGGCTGTGTGGTCCAGCTCGGCCTTCTTTGTAGTGCATG TGACAGCTGAGAGCTTCCTGCTGGCCTCCATGGCCTATGACCGGTTCCTAGCCATCT GTCAACCCCTCCATTATGGTTCTATCATGACCAGGGGACCTGTCTCCAGCTGGTAG CTGTGTCCTATGCATTTGGTGGGCCCAACCAGTCAACACTACTCTGTGACACTACCACCCC CCCTGCCTTTCTGTGGGCCCAACCAGTCCCAACAACAGCCACAGCAAGAGTGGTCCTATGTCTTTT TTCTCCACCTGGCTTGTGCCAACAACAGCCACAGCAAGAGTGGTCCTATGTCTTTT CTGCTCTGGTCACCCTTCTGCCTGCCAGTCATTCTCACCCTCCACTTGCTTGGTCTT GGTGGCCATTGGGAGGAGGATGCGCTCAGTAGCAGGGAGGAGGACCTCCACTT GTGCCTCCCACTTTCTGGCCATTTCTATGCCATTTTCACCTATGT TCAGCCCCATGGATCTACTAACAATACCAATGGCCAAGTAGTGTCCGTCTTCTACAC CATCATAATTCCCATGCTCAATCCCTCATCTATAGCCTCCGCAACAAGGAGGTGAA GGGCGCTCTGCAGAGGAAGCTTCAGGTCAACATCTTTCCCGGCTGAGCCCTGCAAG	MTPGELALASGNHTPVTKFI LQGFSNYPDLQELLFGAILLI YAITVVGNLGMMALIFTDS HLQSPMYFFLNVLSFLDICY SSVVTPKLLVNFLVSDKSISF EGCVVQLAFFVHVTAESF LLASMAYDRFLAICQPLHY GSIMTRGTCLQLVAVSYAF GGANSAIQTGNVFALPFCGP NQLTHYYCDIPPLLHLACA NTATARVVLYVFSALVTLL PAAVILTSYCLVLVAIGRMR SVAGREKDLSTCASHFLAIA IFYGTVVFTYVQPHGSTNNT NGQVVSVFYTIIIPMLNPFIY SLRNKEVKGALQRKLQVNI FPG

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL160314_A	75/76	GCCCATGGGTAACTGGACTGCAGCGGTGACTGAGTTTGTTCTGCTGGGGTTTCCCT GAGCAGGGAGGTGGAGCTGCTGCTCCTCGGTGCTCCTGCTGCCCACGTTCCTGCTGA CTCTTCTGGGGAACCTGCTCATCATCTCCACTGTGCTGTCCCGCCTCCACA CCCCCATGTACTTCTTCTTGTGCAACCTCTCTATCCTGGACATCCTCTTCACCTCAGT CATCTCCAAAAGTGTTGGCCAACTTAGGATCTAGGGATAAAACCATCTCCTTTGC CGGATGTATCACCCAGTGCTATTTCTACTTTTTCTTGGGCACAGTTGAGTTCCTCCT GCTGACGGTCATGTCCTATGACCGGTTATGCCACCATCTGCTGCCCCCTGCGGTACAC CACCATCATGAGAGACCTTCGTCTGCATTGGGACCGTTGTATTCTCTTGGGTGGGAGG CTTCCGTGTCTGTCTTTCCAACCATCCTCATCTCCCAGCTGCCCTTCTGTGGCTCC AATATCATTAACCACTTCTTCTGTGACAGTGGACCCTTGCCGCCCTGGCCTGTGCA GACACCACTGCCATCGAGCTGATGGATTTTATGCTTTCTTCCATGGTCATCCTGC TGCATAGTCCTGTGGCCTATTCCTATACGTACATCATCTTGACCATAGTGCGCATT CCTTCTGCAAGTGGAAGGAAGGAAGAGGCCTTTAATACCTGTGCTTCCCACCTGACCATA GTCATCATTCCTAGTGGCATCACTGTGTTTATCTATGTGACTCCCCTCCAGAAAGAA TATCTGGAGATCAACAAGATCCCTTGGTTCTGAGCAGTGTGGTGACTCCATTCCTC AACCCCTTTATATATACTCTGAGGAATGACACAGTGCAGGGAGTCCTCAGGGATGT GTGGGTCAGGGTTCGAGGAGTTTTGAAAAGAGGATGAGGGCAGTGCTGAGAAGC AGATTATCCTCCAACAAAGACCACCAAGGAAGGGCTTGCTCTTCTCCACCATGTGTC TATTCTGTAAAGCTCCAGTGTTAGAAAAGAGAGAGGAGCTGCCTTA	MGNWTAAVTEFVLLGFSLS REVELLLVLLLPTFLLTLL GNLLIISTVLSCSRLHTPMYF FLCNLSILDILFTSVISPKVLA NLGSRDKTISFAGCITQCYF YFFLGTVEFLLLTVMSYDR YATICCPLRYTTIMRPSVCIG TVVFSWVGGFLSVLFPTILIS QLPFCGSNIINHFFCDSGPLL ALACADTTAIELMDFMLSS MVILCCIVLVAYSYTYIILTI VRIPSASGRKKAFNTCASHL TIVIIPSGITVFIYVTPSQKEY LEINKIPLVLSSVVTPFLNPFI YTLRNDTVQGVLRDVWVR VRGVFEKRMRAVLRSRLSS NKDHQGRACSSPPCVYSVK LQC

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002509_B	77/78	GTATTGTAATTAACCACCATTTGAAATACATGGTGAATAGAAACAATGTGACAGAG TTTATTCTACTGGGGCTTAGAATCCAAAAATGCAGAAAAATCATATTTGTTGTGTTTT GTCATCTACATCACCACCATGATAGGAAATGTGCTCATTGTGGTCACCGTCACTGCC AGCCCATCATTGAGGTCCCCCATGTACTTTTACCTGGCCTATCTGTCCTTTATTGATG CCTGCTATTCCTCCGTCAATGCCCCTAAGCTACACAGATTCACTCTATGAAAACA AGACTATCTTACTCAATGGATGTATGACTCAAGTCTTTGGAGAACATTTTTCGGAG GTGTTGAGGTCATCCTACTTACTGTAATGGCCTATGACCGCTACGTGGTCATCTGCA AGCCCCTTGCACTATACCACCATCATGAAGCAGCATGTTTGTAGCCTGCTAGTGGGA GTGTCATGGGTAGGAGGCTTTCTTCATGCAACCGTACAGATCCTCTTCATCTTCCAA TTACCTTTCTGTGGTCCTAATGTCATAGATCACTTATGTGGGATCTCAACCCTTTGC TCAATCTTGTCTGCACTAATACCCACACTCTAGGACTCTTCGTTGCTGCCAACAGTG GGTTCATATGCCTGTTAAACTTTCTCTTGCTCCTGGTCTCCTATATGGTCATACTGTA CTCCTTAAGGACCCACAGCTTAGAGGCAAGGTGCAAAGCCCTCTCCACCTGTGTCTC CCACATCACAGTTGTCATCTTATTCTTTATACCCTGCATATTTGTGTACATGAGACCT CCAGCTACTTTACCCATTGATAAAGCAGTTGCTGTATTCTACACTATGATAGCTCCT ATGTTAAACCCCTTAATCTACACCCTTGAGGAATGCTCAGATGAAAAATGCCATTAG GAAATTGTGTAGTAGGAAAGCTATTTCAAGTGTCAAATAAAT	MVNRNNVTEFILLGLRIQKC RKSYLLCFVIYITTMIGNVLI VVTVTASPSLRSPMYFYLA YLSFIDACYSSVNAPKLITDS LYENKTILLNGCMTQVFGE HFFGGVEVILLTVMAYDRY VVICKPLHYTTIMKQHVCSL LVGVSWVGGFLHATVQILFI FQLPFCGPNVIDHFMWDLN PLLNLVCTNTHTLGLFVAA NSGFICLLNFLLLVSYMVIL YSLRTHSLEARCKALSTCVS HITVVILFFIPCIFVYMRPPA TLPIDKAVAVFYTMIAPML NPLIYTLRNAQMKNAIRKL CSRKAISSVK

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP002407_A	79/80	GGGATGACTAGCCGCTCTGTGTGTGAGAAGATGACCATGACAACGGAGAACCCCAA CCAGACTGTGGTGAGCCACTTCTTCCTGGAGGGTTTGAGGTACACCGCTAAACATTC TAGCCTCTTCTTCCTCCTCTTCCTCCTCATCTACAGCATCACTGTGGCTGGGAATCTC CTCATCCTCCTAACTGTGGGCTCTGACTCTCACCTCAGCTTACCCATGTACCACTTCC TGGGGCACCTCCTTCCTGGATGCCTGTTTGTCTACAGTGACAGTGCCCAAGGTCA TGGCAGGCCTGCTGACTCTGGATGGGAAGGTGATCTCCTTTGAGGGCTGTGCCGTA CAGCTTTATTGCTTCCACTTTCTGGCCTATCTGTCAACCCCTGCACTACCCAGTGAAC GCCTATGACCGGCTATCTGCTATCTGTCAACCCCTGCACTACCCAGTGGCCATGAAC AGAAGGATGTGTGCAGAAATGGCTGGAATCACCTGGGCCATAGGTGCCACGCACGC TGCAATCCACACCTCCCTACCTTCCGCCTGCTCTACTGTGGGCCTTGCCACATTGC CTACTTCTTCTGCGACATACCCCCTGTCCTAAAGCTCGCCTGTACAGACACCACCAT TAATGAGCTAGTCATGCTTGCCAGCATTGGCATCGTGGCTGCAGCTGTGTTGCGCAG CATCGTTATTTCCTACATCTTCATCGTGCAGCTGTGTTGCGCATCCGCACAGCCCA GGGCCGGCAGCGGCCTTCTCCCCCTGCCCAGCTCACTGGGGTGCTCCTGTA CTACGTGCCACCTGTCTGTATCTACCTGCAGCCTCGCCAGTGAGGCAGGAGCTGG GGCCCCTGCTGTCGTCTTCTACACAATCGTAACTCCAATGCTCAACCCATTCATTACAC TTTGCGGAACAAGGAGGTGAAGCATGCTCGCAAAGGCTTTTGTGCAGCAGCTTCC GAGAGTCTACAGCAGGAGGCAGCCCACCCCCATAGTCTGTGTCTATCAAAACTCACAATTT GCCTGCCAGGAAAGCAACTATTCACATC	MTSRSVCEKMTMTTENPNQ TVVSHFFLEGLRYTAKHSSL FFLLFLLIYSITVAGNLLILLT VGSDSHLSLPMYHFLGHLSF LDACLSTVTVPKVMAGLLT LDGKVISFEGCAVQLYCFHF LASTECFLYTVMAYDRYLA ICQPLHYPVAMNRRMCAE MAGITWAIGATHAAIHTSLT FRLLYCGPCHIAYFFCDIPPV LKLACTDTTINELVMLASIG IVAAGCLILIVISYIFIVAAVL RIRTAQGRQRAFSPCTAQLT GVLLYYVPPVCIYLQPRSSE AGAGAPAVFYTIVTPMLNP FIYTLRNKEVKHALQRLLCS SFRESTAGSPPP

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL391156_B	81/82	CTTGGAACCATGGATAAGTCCAATTCTTCAGTGGTGTCTGAATTTGTACTGTTGGGA CTCTGTAGTTCTCAAAAACTCCAGCTTTTCTATTTTGTTTCTTCTCTGTGTGTATA CAGTCATTGTGCTGGGAAATCTTCTCATTATCCTCACAGTGACTTCTGATACCAGCC TGCACTCCCCTATGTACTTTCTTGGGAAACCTTTCCTTTGTGACATTTGTCAGGC TTCTTTTGCTACCCCTAAAATGATTGCAGATTTTCTGAGTGCACACGAGACCATATC TTTCAGTGGCTGCATAGCCCAAATTTTCTTTATTCACCTTTTTACTGGAGGGGAGAT GGTGCTACTTGTTTCGATGGCCATGACCAGGTATGTAGCCATATGCAAACCCTTATA CTATGTGGTCATCATGAGCCGAAGGACATGCACTGTTCTTGGTAATGATCTCCTGGGC TGTGAGCTTGGTGCACACATTAAGCCAGTTATCATTTACTGTGAACCTGCCTTTTTG TGGACCTAATGTAGTAGACAGCTTTTTTGTGATCTTCCTGCAGTCACCAAACTTGC CTGCCTGGACTCTTACATCATTGAAATACTAATTGTGGTCAATAGTGGAATTCTTTC CCTAAGCCACTTTCTCTCTTGGTCAGCTCCTACATCATTATTCTTGTTACAGTTTGG CTCAAGTCTTCAGCTGCAATGGCAAAGGCATTTTCTACGCTGGCTTCCCATATTGCA GTAGTAATATTATTCTTTGGACCTTGCATCTTCATCTATGTGTGGCCCTTTACCATCT CTCCTTTGGATAAATTTCTTGCCATATTTACACTGTTTTCACCCCCGTCCTAAACCC CATTATTTATACACTAAGGAATAGGGATATGAAGGCTGCCGTAAGGAAAATTGTGA ACCATTACCTGAGGCCAAGGAGCCAAGGAGAATTTCTGAAAGTGTCACTAGTAGTGAGAACTTCC TTTCATTAAGACAAAACTCCTTCAAATTCCTCAG	MDKSNSSVVSEFVLLGLCSS QKLQLFYCFFSVLYTVIVL GNLLILTVTSDTSLHSPMYF LLGNLSFVDICQASFATPKM IADFLSAHETISFSGCIAQIFF IHLFTGGEMVLLVSMAYDR YVAICKPLYYVVIMSRRTCT VLVMISWAVSLVHTLSQLS FTVNLPFCGPNVVDSFFCDL PRVTKLACLDSYIIEILIVVN SGILSLSTFSLLVSSYIIILVT VWLKSSAAMAKAFSTLASH IAVVILFFGPCIFIYVWPFTIS PLDKFLAIFYTVFTPVLNPII YTLRNRDMKAAVRKIVNH YLRPRRISEMSLVVRTSFH

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC024399_B	83/84	CTTGGAACCATGGATAAGTCCAATTCTTCAGTGGTGTCTGAATTTGTACTGTTGGGA CTCTGTAGTTCTCAAAAACTCCAGCTTTTCTATTTTGTTCTTCTCTGTGTTGTATA CAGTCATTGTGCTGGGAAATCTTCTCATTATCCTCACAGTGACTTCTGATACCAGCC TGCACTCCCCTATGTACTTTCTCTTGGGAAACCTTTCCTTGTTGGACATTTGTCAGGC TTCTTTTGCTACCCCTAAAATGATTGCAGATTTTCTGAGTGCACACGAGACCATATC TTTCAGTGGCTGCATAGCCCAAATTTCTTTATTCACCTTTTACTGGAGGGGAGAT GGTGCTACTTGTTTGATGGCCTATGACAGGTATGAGCCATATGCAAACCCTTATA CTATGTGGTCATCATGAGCCGAAGGACATGCCACTGTCTTGGTAATGATCTCCTGGGC TGTGAGCTTGGTGCACACATTAGACAGCTTTTTTGTGATCTTCCTGAGTCACCAAACTTGC TGGACCTAATGTAGTAGTAGACAGCTTTTTTGTGATCTTCCTGAGTCACCAAACTTGC CTGCCTGGACTCTTACATCATTGAAATACTAATTGTGGTCAATAGTGGAATTCTTC CCTAAGCACTTTCTCTCTCTTGGTCAGCTCCTACATCATTATTCTTGTTACAGTTGG CTCAAGTCTTCAGCTGCAATGGCAAAGGCATTTCTACGCTGGCTTCCCATATTGCA GTAGTAATATTATTCTTGGACCTTGCATCTTCATCTATGTGTGGCCCTTTACCATCT CTCCTTGGATAAATTTCTTGCCATATTTTACACTGTTTTCACCCCGGTCCTAAACCC CATTATTTATACACTAAGGAATAGGGATATGAAGGCTGCCGTAAGGAAAATTGTGA ACCATTACCTGAGGCCAAGGAGAATTCTGAAATGTCACTAGTAGTGAGAACTTCC TTTCATTAAGACAAAACTCCTTCAAATTCCTCAGGTCAATACACTGTTTAATATTTT AAT	MDKSNSSVVSEFVLLGLCSS QKLQLFYFCFFSVLYTVIVL GNLLILTVTSDTSLHSPMYF LLGNLSFVDICQASFATPKM IADFLSAHETISFSGCIAQIFF IHLFTGGEMVLLVSMAYDR YVAICKPLYYVVIMSRRTCT VLVMISWAVSLVHTLSQLS FTVNLPFCGPNVVDSFFCDL PRVTKLACLDSYIIEILIVVN SGILSLSTFSLLVSSYIIILVT VWLKSSAAMAKAFSTLASH IAVVILFFGPCIFIYVWPFTIS PLDKFLAIFYTVFTPVLNPII YTLRNRDMKAAVRKIVNH YLRPRRISEMSLVVRTSFH

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL356019_D	85/86	CATGAATAACTCACAGATATCTACTGTGACGCAGTTTGTGTTGTTGGGGTTTCCTGG TCCCTGGAAAATTCAGATCATCTTTTTCTCAATGATTTTGTTGGCTCACATCTTCACT CTGACTGGGAATATGGCCATCATCTGTGCAGTGAGGTGGGACCATCGACTCCATAC CCCTATGTACGTGCTCCTAGCCAACTTCTCTTCCTAGAGATCTGGTATGTGACCTG CACAGTCCCAACATGCTGGTAAATTTTTCTCCAAAACTAAGACCATATCATTCTC TGGATGTTTCACTCAGTTCCACTTCTTCTTTCCCTGGGCACAACTGAATGCTTCTTC CTCTGTGTCATGGCTTATGATCGGTACCTGGCCATCTGCCACCCACTGCACTATCCC TCCATTATGACTGGCCAGCTCTGTGGCATCTTGGTGTCTCTTTGTTGGCTCATTGGTT TCCTTGGACATTCAATTTCATTTTCATTTTCTCAACTACCTTTCTGTGGTCCCAA CATCATTGATCATTTTCTGTGTGATGTAGACCCACTGATGGCATTGTCCTCTGCCCC TACTCACATCATAGGGCATGTGTTCCATTCTGTGAGCTCTCTTTCATCAACCTCAC CATGGTGTACATCCTTGGGTCCTATACCCTTGGTGCTCAGAACTGTGCTTAAGGTTCC TTCTTCAGCTGGATGGCAAAAGGCCATCTCTACCTGTGGGTCACACTTGGTTGTTGT GTCTCTGTTCTATGGAGCCATAATGCTGATGTATGTGAGTCCCACACCTGGCAACTC AGTTGCTATGCATAAGCTCATCACACTGATATATTCTGTGTAACACCTGTCTTAAA CCCCCTCATCTCACAGCCTACGCAACAAGGACATGAAATATGCCCTCCATCATGTCTT CTGTGGAATGAGAATTATCCAGAGATCATGAATAGGGTTTTTTATAACCCAAT	MNNSQISTVTQFVLLGFPGP WKIQIIFFSMILLVYIFTLTG NMAIICAVRWDHRLHTPMY VLLANFSFLEIWYVTCTVPN MLVNFFSKTKTISFSGCFTQ FHFFFSLGTTECFFLCVMAY DRYLAICHPLHYPSIMTGQL CGILVSLCWLIGFLGHSISIFF IFQLPFCGPNIIDHFLCDVDP LMALSSAPTHIIGHVFHSVS SLFINLTMVYILGSYTLVLR TVLKVPSSAGWQKAISTCG SHLVVVSLFYGAIMLMYVS PTPGNSVAMHKLITLIYSVV TPVLNPLIYSLRNKDMKYA LHHVFCGMRIIQRS

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL163152_D	87/88	AAATTATGGAAACACAGAACCTCACAGTGGTGACAGAATTCATTCTTCTTGGTCTG ACCCAGTCTCAAGATGCTCAACTTCTGGTCTTTGTGCTAGTCTTAATTTTCTACCTTA TCATCCTCCCTGGAAATTCCTCATCATTTCACCATAAAGTCAGACCCTGGGCTCA CAGCCCCCCTCTATTTCTTTCTGGGCAACTTGGCCTTACTGGCATCCTACTCCTT CATTGTGGTTCCCAGGATGTTGGTGGACTTCCTCCTCGAGAAGAAGGTAATCTCCTA TAGAAGCTGCATCACTCAGCTCTTTTTCTTGCATTTTCTTGGAGGCGGGAGAGATGTT CCTCCTCGTTGTGATGGCCTTTGACCGGCTACATCGCCGCCATCTGCCGGCCTTTACACTA TTCAACCATCATGAACCCTAGAGCCTGCTATGCATTATCGTTGGTTCTGTGGCTTGG GGGCTTTATCCATTCCATTGTACAAGTAGCCCTTATCCTGCACTTGCCTTTCTGTGG CCCAAACCAGCTCGATAACTTCTTCTGTGATGTTCCACAGGTCATCAAGCTGGCCTG CACCAATACCTTTGTGGTGGAGCTTCTCGATGGTCTCCAACAGTGGCCTGCTCAGCCT CCTGTGCTTCCTGGGCCTTCTGGCCTCCTATGCAGTCATCCTCCTGTGTCGTATAAGGGA GCACTCCTCTGAAGGAAAGAGCAAAGGCTATTTCCACATGCACCACCCATATTATCAT TATATTTCTCATGTTTGGACCTGCTATTTTCATCTACACTTGCCCCCTTCCAGGCTTTC CCAGCTGACAAGGTAGTTTCTCTTTTCTTTCCATACTGTCATCTTTCCTTTGATGAACCCTG TTATTTATACGCTTCGCAACCAGGAGGTGAAAGCTTCCATGAGGAAGTTGTTAAGT CAACATATGTTTTGCTGAATAGAAAGAGAAAAAGCAAGAACGGAGAAA	METQNLTVTEFILLGLTQS QDAQLLVFVLVLIFYLILPG NFLIIFTIKSDPGLTAPLYFFL GNLALLDASYSFIVVPRMLV DFLSEKKVISYRSCITQLFFL HFLGAGEMFLLVVMAFDRY IAICRPLHYSTIMNPRACYA LSLVLWLGGFIHSIVQVALIL HLPFCGPNQLDNFFCDVPQ VIKLACTNTFVVELLMVSNS GLLSLLCFLGLLASYAVILC RIREHSSEGKSKAISTCTTHII IIFLMFGPAIFIYTCPFQAFPA DKVVSLFHTVIFPLMNPVIY TLRNQEVKASMRKLLSQH MFC

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL356019_A	89/90	AAATTATGGAAACACAGAACCTCACAGTGGTGACAGAATTCATTCTTCTTGGTCTG ACCCAGTCTCAAGATGCTCAACTTCTGGTCTTTGTGCTAGTCTTAATTTTCTACCTTA TCATCTCCCTGGAAATTCCTCATCATTTTCACCATAAAGTCAGACCCTGGGCTCA CAGCCCCCCCTCTATTTCTTTCTGGGCAACTGGCCTTACTGGATGCATCCTACTCCTT CATTGTGGTTCCCAGGATGTTGGTGACTTCCTCTGAGAAGAAGGTAATCTCCTA TAGAAGCTGCATCACTCAGCTCTTTTCTTGCATTTCTTGGAGCGGGAGAGATGTT CCTCCTCGTTGTGATGGCCTTTGACCGCTACATCGCCATCTGCCGGCCTTTACACTA TTCAACCATCATGAACCCTAGAGCCTGCTATGCATTATCGTTGGTTCTGTGGCTTGG GGGCTTTATCCATTCCATTGTACAAGTAGCCCTTATCCTGCCCTTTCTGTGG CCCAAACCAGCTCGATAACTTCTTCTGTGATGTTCCACAGTCAGTCATCAAGCTGGCCTG CACCAATACCTTTGTGGTGGAGCTTCTGATGGTCTCCAACAGTGGCCTGCTCAGCCT CCTGTGCTTCCTGGGCCTTCTGGCCTCCTATGCCAGTCATCCTCTGTGTATAAGGGA GCACTCCCTCTGAAGGAAGGAAAGAGCAAGGCTATTTCCACATGCACCACCATATTATCAT TATATTTCTCATGTTTGGACCTGCTATTTCATCTCACACTGCCCCTTCCAGGCTTTC CCAGTGCACAAGGTAGTTTCTCTTTTCCATACTGTCATCTTTCTTTGATGAACCCTG TTATTTATACGCTTCGCAACCAGGAGGTGAAAGCTTCCATGAGGAAGTTGTTAAGT CAACATATGTTTTGCTGAATAGAAGAGAAAGCAAGAACGGGAGAAA	METQNLTVVTEFILLGLTQS QDAQLLVFVLVLIFYLIILPG NFLIIFTIKSDPGLTAPLYFFL GNLALLDASYSFIVVPRMLV DFLSEKKVISYRSCITQLFFL HFLGAGEMFLLVVMAFDRY IAICRPLHYSTIMNPRACYA LSLVLWLGGFIHSIVQVALIL HLPFCGPNQLDNFFCDVPQ VIKLACTNTFVVELLMVSNS GLLSLLCFLGLLASYAVILC RIREHSSEGKSKAISTCTTHII IIFLMFGPAIFIYTCPFQAFPA DKVVSLFHTVIFPLMNPVIY TLRNQEVKASMRKLLSQH MFC

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC016856_A	91/92	CTCTCACTGCCACATATGCAACCATATACCAAAAACTGGACCCAGGTAACTGAATTT GTCATGATGGGCTTTGCTGGCATCCATGAAGCACACCTCCTCTTCTTCATACTCTTC CTCACCATGTACCTGTTCACCTTGGTGGAGAATTTGGCCATCATTTTAGTGGTGGGT TTGGACCACCGACTACGGAGACCCATGTATTTCTTCCTGACACACTTGTCCTGCCTT GAAATCTGGTACACTTCTGTTACAGTGCCCAAGATGCTGGCTGGTTTTATTGGGGTG GATGGTGGCAAGAATATCTCTTATGCTGGTTGCCTATCCCAGCTCTTCATCTTCACC TTTCTTGGGGCAACTGAGTGTTTCCTACTGGCTGCCATGGCCTATGATCGTTATGTG GCCATTTGTATGCCTCTCCACTATGGGCTTTGTGTCCTGGGGCACCTGCATCCGT CTGGCAGCTGCCTGTTGGCTGGTAGGTTTCCTCACACCATCTTGCCAATCTACCTC TTGTCTCAGCTAACATTTTGTGGCCCAAATGTCATTGACCATTTCTCCTGTGATGCC TCACCCTTGCTACCTGTCGTGCTCAGATGTCACTTGGAAGGAGACTGTGGATTTC CTGGTGTCTCTGGCTGTGCTACTGGCCTCCTATGGTCATTGCTGTGTCCTATGGC AACATCGTCTGGACACTGCTGCACATCCGCTCAGCTGCTGAGCGGCTGGAAGGCCTT CTCTACCTGTGCAGCTCACCTGACTGTGGTGAGCCTCTTCTATGGCACTCTTTTCTTT ATGTATGTCCAGACCAAGGTGACCTCCTCCATCAACTTCAACAAGGTGTATCTGTC TTCTACTCTGTTGTCACGCCCATGCTCAACCCTCTCATCTACAGTCTTAGGAACAAG GAAGTGAAGGGAGCTCTGGGTCGAGTCTTTTCTCTCAACTTTTGGAAGGGACAGTG AGGAGGCAG	MQPYTKNWTQVTEFVMMG FAGIHEAHLLFFILFLTMYLF TLVENLAIILVVGLDHRLRR PMYFFLTHLSCLEIWYTSVT VPKMLAGFIGVDGGKNISY AGCLSQLFIFTFLGATECFLL AAMAYDRYVAICMPLHYG AFVSWGTCIRLAAACWLVG FLTPILPIYLLSQLTFCGPNVI DHFSCDASPLLALSCSDVT WKETVDFLVSLAVLLASSM VIAVSYGNIVWTLLHIRSAA ERWKAFSTCAAHLTVVSLF YGTLFFMYVQTKVTSSINFN KVVSVFYSVVTPMLNPLIYS LRNKEVKGALGRVFSLNFW KGQ

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022882_F	93/94	CCAACAATACAAATGGCTTCAGGAAATCTCACATGGGTGACGGAGTTCATTCTTGT GGGAGTCTCAGATGATCCGGAGCTCCAGATTCCCCTCTTCCTGGTCTTCCTGGTGCT CTATTTGCTGACCGTGGCAGGGAACCTGGGCATCATCACCCTCACCAGTGTTGACCC TCAACTTCAAACCCCCATGTACTTTTTCCTCAGACACTGGCTATTATTAATCTTTGC AATTCTACTGTCGTTGCCCCTAAAATGCTGGTTAACTTCCTGGTTACCAAGAAAACC ATATCATACTATGGATGTGCAGCCAACTGGGTGGATTCTTGGTTTCATTGTGGCT GAGATTTTCACGCTGGCTGCAATGGCCTATGACCGCTATGTGGCTATTTGGAGCCCT CTGCTCTACGCCGTAGTGGTGTCTCCAAAGGTGTGCGTCTGCTGCTGGTGCCCTCACA TACCTTCAGAGTCTTATCACGACCACTGACGTGTCTCTCTGTGTTCTCTGTGTCAT ACTGTTCTTCCAACATTATCAACCATTTTACTGTGATGATGTCCCTTTGCTAGCATT GTCCTGTTCTGATACCTACATTCCAGAAACAGCAGTCTTTATCTTTTCAGGGACCAA CTTGCTTTTCTCCATGATCGTTGTTCTGATATCCTACTTCAACATTGTTATTACCATT TTGAGGATACGTTCCTCAGAAGGACGACAAAAAGCCTTTCCACCTGTGCTTCTCAC ATGATAGCTGTGGTTGTTCTATGGGACTCCTCCTTTTCATGTATTTGCAACCAAGG AGTAATCATTCATTAGATACTGACAAAATGGCTTCGGTCTTCTCACACCCTGGTGATA CCAGTGCTGAACCCTCTAATCTACAGCCTCAGGAACAAGAACGTGAAGGATGCACT AAAGAGGTTCCTAGATAACCCATGCCGATCACTCACTCAAACTAATGTAAAT	MASGNLTWVTEFILVGVSD DPELQIPLFLVFLVLYLLTV AGNLGIITLTSVDPQLQTPM YFFLRHLAIINLCNSTVAP KMLVNFLVTKKTISYYGCA AQLGGFLVFIVAEIFTLAAM AYDRYVAIWSPLLYAVVVS PKVCRLLVSLTYLQSLITAL TVSSCVFSVSYCSSNIINHFY CDDVPLLALSCSDTYIPETA VFIFSGTNLLFSMIVVLISYF NIVITILRIRSSEGRQKAFSTC ASHMIAVVVFYGTLLFMYL QPRSNHSLDTDKMASVFYT LVIPVLNPLIYSLRNKNVKD ALKRFLDNPCRSLKLM

135

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022882_E	95/96	ATGAATCATGTGGTAAAACACAATCACACGGCAGTGACCAAGGTGACTGAATTTAT TCTCATGGGGATTACAGACAACCCTGGGCTGCAGGCTCCACTGTTTGGACTCTTCCT CATCATATATCTGGTCACAGTGATAGGCAATCTGGGCATGGTTATCTTGACCTACTT GGACTCCAAGCTACACACCCCCATGTACTTTTTCCTTAGACATTTGTCAATCACTGA TCTTGGTTACTCCACTGTCATTGCCCCGAAGATGTTAGTAAACTTCATAGTGCACAA AAACACAATTTCTTACAATTGGTATGCCACTCAGCTAGCATTCTTTGAGATTTTCAT CATCTCTGAGCTCTTTATTCTATCAGCAATGGCCTATGATCGGCTAGCGTACGTAGCCATCTG TAAACCTCTTCTGTACGTGATCATCATGGCAGAGAAAGTACTTGGGTGGTGTAAT TGTTCCCTATCTCTATAGCACGTTTGTGTCACTATTTCTCACAATTAAGTTATTTAAA CTGTCCTTCCTGTGGCTCAAACATAATCAGCTATTTTTACTGTGACTGTATCCCTCTGA TGTCCATACTCGTGTTCTGACACAAATGAATTAATAATTTTGATCTTCTCAG GCTGTAATTTGCTCTTCTCCCCTCAATTGTTCTCATATCCTACACATGTTTATTCTAGT GGCCATTCTCAGAATGAACTCAAGGAAAGGGAGGTACAAAGCCTTCCCACCTGTA GCTCTCATCTGACAGTGGTGATCATGTTCTATGGGACACATTGTTATTATTTACTTGC AACCCAAGTCCAGTCATACTTTGGCTATTGATAAAATGGCCTCAGTGTTTTATACCC TGTTGATTCCTATGCTGAATCCGTTGAATCCGTTGATCTACAGCCTAAGGAACAAAGAAGTAAAA GATGCTCTAAAAGAGAACTTTAACCAATCGATTCAAAATTCCCATTTAATATCTTAAT ACTCA	MNHVVKHNHTAVTKVTEFI LMGITDNPGLQAPLFGLFLII YLVTVIGNLGMVILTYLDSK LHTPMYFFLRHLSITDLGYS TVIAPKMLVNFIVHKNTISY NWYATQLAFFEIFIISELFILS AMAYDRYVAICKPLLYVII MAEKVLWLVIVPYLYSTF VSLFLTIKLFKLSFCGSNIISY FYCDCIPLMSILCSDTNELEL IILIFSGCNLLFSLSIVLISYMF ILVAILRMNSRKGRYKAFST CSSHLTVVIMFYGTLLFIYL QPKSSHTLAIDKMASVFYTL LIPMLNPLIYSLRNKEVKDA LKRTLTNRFKIPI

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022882_C	97/98	CAATTGAACACATCATGGGTAGAAGAAATAACACAAATGTGCCTGACTTCATCCTTAC GGGACTGTCAGATTCTGAAGAGGTCCAGATGGCCCTCTTTATACTATTTCTCCTGAT ATACCTAATTACTATGCTGGGCAATGTGGGGATGATATTGATAATCCGCCTGGACCT CCAGCTTCACACTCCCATGTATTTTTCCTTACTCACTTGTCATTTATTGACCTCAGT TACTCAACTGTCATCACACCTAAAACCTTAGCGAACCTTACTGACTTCCAACTATATT TCCTTCAATGGGCTGCTTGCCCAGATGTTCTTTTTGTCTTCTTGGGAGCTGCTGAAT GTTTTCTTCTCTCATCAATGGCCTATGATCGCTACGTAGCTATCTGCAGTCCTCTACG TTACCCAGTTATTATGTCCAAAAGGCTGTGTTGCGCTCTGTTCCACTGGGCCCTATGT GATTAGCTTTATCAACTCCTTTGTCAATGTGGTTTGGATGAGCAGACTGCATTTCTG CGACTCAAATGTAGTTCGTCACTTTTTCTGCGACACGTCTCCAATTTTAGCTCTGTCC TGCATGGACACATACGACATTGAAATCATGATACACATTTAGCTGGTTCCACCCTG ATGGTGTCCCTTATCACAATATCTGCATCCTATGTGTCCATTCTCTCTACCATCCTGA AAATTAATTCCACTTCAGGAAAGCAGAAAGCTTTGTCTACTTGTCCCTCCATCTCT TGGGAGTCACCATCTTTTATGGAACTATGATTTTTACTTATTTATTATACTATTGTGATTCCCAT CTTATTCTTGGGAAGGGATCAAGTGGCTTCGTTAGAAACCAAGAAGAAGT GCTGAATCCACTCATTTATAGTCTTAGAAAACAAAGAAGTTAAAAATGCTCTCATTAG AGTCATGCAGAGAAGACAGGACTCCAGGTAATTAAAATAGCAGGAATGCTGAACAT TTAAAACTCATCTTTTCTTTCTTTCTATTTG	MGRRNNTNVPDFILTGLSDS EEVQMALFILFLLIYLITMLG NVGMILIRLDLQLHTPMYF FLTHLSFIDLSYSTVITPKTL ANLLTSNYISFMGCFAQMFF FVFLGAAECFLLSSMAYDR YVAICSPLRYPVIMSKRLCC ALVTGPYVISFINSFVNVVW MSRLHFCDSNVRHFFCDT SPILALSCMDTYDIEIMIHIL AGSTLMVSLITISASYVSILS TILKINSTSGKQKALSTCAS HLLGVTIFYGTMIFTYLKPR KSYSLGRDQVASVFYTIVIP MLNPLIYSLRNKEVKNALIR VMQRRQDSR

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022882_B	99/100	TAAAAACTGAAATGGACAAGTTGTCATCAGGTTTGGATATATACAGGAATCCACTG AAGAACAAGACTGAAGTCACCATGTTTATATTGACAGGCTTCACAGATGATTTTGA GCTGCAAGTCTTCCTATTTTTACTATTTTTTGCAATCTATCTCTTTACCTTGATAGGC AATTTAGGGCTGGTCTGTGTTGGTCATTGAGGATTCCTGGCTCCACAACCCATGTAT TATTTTCTTAGTGTTTTATCATTCTTGGATGCTTGCTATTCTACAGTTGTCACTCCAA AAATGTGGTCAATTCCTGGCAAAAAATAAATCCATTTCATTTATCGGATGTGCAA CACAGATGCTTCTTTTTGTTACTTTTGGAACTACACAGAAATGTTTTCTTCTTGGCTGCAAT GGCTTATGATCACTATGTAGCCATCTACAACCCTCTCCTGTATTCAGTGAGCATGTC ACCCAGAGTCTATGTGCCACTCACTGCTTCCTACGTTGCTGGCATTTTACATGC TACTATACATATAGTGGCTACACATTTAGCCTGCTGTCCTTCCTGTGGATCCAATGAAATTAG GCATGTCTTTTGTGATATGCCTCCTCCTGCTATTCTTTGTTCTGACACTCACACA AACCAGCTTCTACTCTTCTACTTTGTGGGTTCTATTGAGATAGTCACTATCCTGATT GTCCTCATTTCCTGTGATTTCATTCTTGTTGTCATTCTGAAGATGCATTCTGCTAAGG GAAGGCAAAAGGCCTTCTCTACATGTGGCTCTCACCTAACTGGAGTGACAATTTATC ATGGAACAATTCTCGTCAGTTATATGAGACCAAGTTCCAGCTATGCTTCAGACCATG ACATCATAGTGTCAATATTTTACACAATTGTGATTCCCAAGTTGAATCCCATCATCT ATAGTTTGAGGAACAAAGAAGTAAAAAAGGCAGTGAAGAAAATGTTGAAAATTGGT TTACAAATGAAGAATAATATTTAAAAATTGA	MDKLSSGLDIYRNPLKNKT EVTMFILTGFTDDFELQVFL FLLFFAIYLFTLIGNLGLVVL VIEDSWLHNPMYYFLSVLSF LDACYSTVVTPKMLVNFLA KNKSISFIGCATQMLLFVTF GTTECFLLAAMAYDHYVAI YNPLLYSVSMSPRVYVPLIT ASYVAGILHATIHIVATFSLS FCGSNEIRHVFCDMPPLLAI SCSDTHTNQLLLFYFVGSIEI VTILIVLISCDFILLSILKMHS AKGRQKAFSTCGSHLTGVTI YHGTILVSYMRPSSSYASDH DIIVSIFYTIVIPKLNPIIYSLR NKEVKKAVKKMLKLVYK

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022207_C	101/102	GTTTCTACCATGGGTGACAGGGGAACAAGCAATCACTCAGAAATGACTGACTTCAT TCTTGCAGGCTTCAGGGTACGCCCAGAGCTCCACATTCTCCTCTTCCTGCTATTTTTG TTTGTTTATGCCATGATCCTTCTAGGGAATGTTGGGATGACCATTATTATGACT GATCCTCGGCTGAACACACCAATGTATTTTTTCCTAGGCAATCTCTCCTTCATTGAT CTTTCTATTCATCTGTTATTGAACCCAAGGCTATGATCAACTTCTGGTCTGAAAAC AAGTCTATCCTTTGCAGGCTGTGTGGCCCAGCTCTTTCTCTTGCCCTCCTCATTG TGACTGAGGGATTTCTCCTGGCGGCCATGGCTTATTGACCCGCTTATTGCCATCTGCA ACCCTCGCTCTACTCTGTTCAAATGTCCACACGTCTGTGTACTCAGTTGGTGGCTG GTTCCTATTTTTGTGGCTGCATTAGCTCAGTTATTCAGACTAGCATGACATTTACTTT ATCTTTTTGCGCTTCTCCGGCGTGTTCTGATCTCTTTATCCATAGAATGATATCTTT AGAGTGTCTTGTTCTGCCTACTATCATAGTCATTATAGTATCTTACACATGTATATT TTATTATCTTGCCTACTATCATAGTCATTATAGTATCTTACACATGTATATTGTGTCCAC AGTTCTAAAGATACATTCTACTGAGGGACATAAGAAGGCCTTCTCCACCTGCAGCTC TCACCTGGGAGTGTGAGTGCTGTATGGTGCTGTCTTTTTATGTATCTCACTCC TGACAGATTTCCTGAGCTGAGTAAAGTGGCATCCTTATGTTACTCCCTAGTCACTCC CATGTTGAATCCTTTGATTTACTCTGAGGAACAAAGATGTCCAAGAGGCTCTAAA AAAATTTCTAGAGAGAAGAAAATATTATTCTTTGATTATTATTTCTCTTTCACCAATTT TATT	MGDRGTSNHSEMTDFILAG FRVRPELHILLFLLFLFVYA MILLGNVGMMTIIMTDPRL NTPMYFFLGNLSFIDLFYSS VIEPKAMINFWSENKSISFA GCVAQLFLALLIVTEGFLL AAMAYDRFIAICNPLLYSVQ MSTRLCTQLVAGSYFCGCIS SVIQTSMTFTLSFCASRAVD HFYCDSRPLQRLSCSDLFIH RMISFSLSCIIILPTIVIIVSY MYIVSTVLKIHSTEGHKKAF STCSSHLGVVSVLYGAVFF MYLTPDRFPELSKVASLCYS LVTPMLNPLIYSLRNKDVQE ALKKFLEKKNIIL

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022207_B	103/104	GTTCTTGCCATGGGTGACAAGGGAACAGGCAACCATTCAGATGTAACTGATTTCAT TCTTGAAGGCTTCAGGGTCCGCCCCAGAGTTCTACATTCTCCTTCTTCCTGTTCCTG CTGATCTATAGCATGGTTCTTTGGGGAACATTAGTGTGATGACAATCATTGTAACT GATTCCCAGCTGAACACACCAATTGTATTTTTTCTAGGCAACCTCTCCTTCATTGAC GTCTCCTACTCCACTGTTATTGCTCCTAAAGCCATGGCCCACTTCCTGTCTGAAAAA AAGACAGTCTCTTTGCAGGTTGTGTGTGCCCCAGTTATTCCTTTTGCCCGTGTTCATTG TAACAGAGGGGTTTGTCCTGGCAGCCATGGCCTATGACCGGCCTCAGTGCCATCTGCA ATCCTCCTTCTTCATAGTGTTCACATGTCAAGAGCGCCTCTGCACTCAGTTGGTTGCTG GTTCTTATTTCTGTGGCTGGGCCAGTTCCATCCTCCAAGTCAGTGTAACATTCTCAG TGTCCTTCTGTGCTTCCAGAGTCATTGCTCACTTCTACTGTGATTCTTATCAAATTGA AAAGATTTCCTGTTCTAATCTCTTTGTCAATAAGATGGTATCTCTGAGTTTGAGTGT CATCATTATTTTGCCTACAATTGTTGTTATTATAGTATCTTACCTGTATATTGTATCC TCAGTCTTGAAGATCCCCTCCAGTGAAGGGAGAAAGAACTTTTCCACTTGCAG CTCCCATCGGGGTGTTGTAAGTTTGCTCCAAGGGACTGTTTCCTTTGTGTACCTCAC ACCTCCAAGCAATCCTGAACTTCGCAAAGTGGCTTCAGTATTTACATATGTGTTAC ACCCATGTTAAACCCTGTTGTAACAAAAAGCTTTATCCTAATTCCTACTTCCTTATGATTTC GAGAAAATCCTGGTAACAAAAAAGCTTTATCCTAATTCCTACTTCCTTATGATTTC CTCATTAATGG	MGDKGTGNHSDVTDFILEG FRVRPEFYILLFFLFLLIYSM VLLGNISVMTIIVTDSQLNT PMYFFLGNLSFIDVSYSTVI APKAMAHFLSEKKTVSFAG CVAQLFLFALFIVTEGFVLA AMAYDRFSAICNPLLHSVH MSRRLCTQLVAGSYFCGWA SSILQVSVTFSVSFCASRVIA HFYCDSYQIEKISCSNLFVN KMVSLSLSVIIILPTIVVIIVS YLYIVSSVLKIPSSEGRKKDF STCSSHRGVVSLLQGTVSFV YLTPPSNPELRKVASVFYIC VTPMLNPLIYSLRNKDVKE ALRKILCNKKALS

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC011879_A	105/106	GATGATGAGTAACCAGACGTTGGTAACCGAGTTCATCCTGCAGGGCTTTTCGGAGC ACCCAGAATACCGGGTGTTCTTATTCAGCTGTTTCCTTCCTCTACTCTGGGGCCCT CACAGGTAATGTCCTCATCACCTTGGCCATCACGTTCAACCCTGGCTCCACGCTCC TATGTACTTTTTCTTACTCAACTTGGCTACTATGGACATTATCTGCACCTCTTCCATC ATGCCCCAAGGCGCTGGCCAGTCTGGTGTCGGAAGAGAGCTCCATCTCCTACGGGGG CTGCATGGCCCAGCTCTATTTCCTCACGTGGGCTGCATCCTCAGAGCTGCTGCTCCT CACGGTCATGGCCTATGACCGGTACGGCAGCCATCTGCCACCCGGCTGCATTACAGCA GCATGATGAGCAAGGTGTTCTGCAGCGGGCTGGCCACAGCCGTGTGGCTGCTCTGC GCCGTCAACACGGCCATCCACACGGGGCTGATGCTGCGCTTGGATTTCTGTGGCCCCT AATGTCATTATCCATTTCTTCTGCGAGGTCCCCCTGCTCCTGCTCTCCTGCAGCT CCACCTACGTCAACGGTGTCATGATTGTCCTGGCGGATGCTTTCTACGGCATAGTGA ACTTCCTGATGACCATCGCGTCTATGGCTTCATCGTCCTCCAGCATCCTGAAGGTGA AGACTGCCTGGGGGAGGCAGAAAGCCTTCTCCACCTGCTTCTTCCCACCTCACCGTGG TGTGCATGTATTACACCGCTGTCTTCTACGCCTACATAAGCCCGGTCTCTGGCTACA GCGCAGGGAAGAGCAAGTTGGCTGGCTGCTGTACACTGTGCTGTGAGTCCTACCCCTC AACCCCTCATCTATCTACTTTGAGAAACAAGGAGGTCAAAGCAGCCCCTCAGGAAGCT TTTCCCTTTCTTCAGAAATTAACTT	MMSNQTLVTEFILQGFSEHP EYRVFLFSCFLFLYSGALTG NVLITLAITFNPGLHAPMYF FLLNLATMDIICTSSIMPKAL ASLVSEESSISYGGCMAQLY FLTWAASSELLLTVMAYD RYAAICHPLHYSSMMSKVF CSGLATAVWLLCAVNTAIH TGLMRLRLDFCGPNVIIHFFC EVPPLLLSCSSTYVNGVMI VLADAFYGIVNFLMTIASYG FIVSSILKVKTAWGRQKAFS TCSSHLTVVCMYYTAVFYA YISPVSGYSAGKSKLAGLLY TVLSPTLNPLIYTLRNKEVK AALRKLFPFFRN

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC011571_A	107/108	GTACTGATTATGCCACTGTCTCATGCCCAACCAGAGCTGCCCAGAAACAGTTCATCTTA CTGGGTTTCTCAGGCAGACCCAGGCTGGAGCATGTCCTCTTGTGTTTGTCCTCATC TTCTACCTTGTGACCTTAGTGGGCAACATCATCATTATCTTGATCTCCACCTGGAC CCCTGCCTCCACATGCCCATGTACTTCTTCCTCACTAACTTGTCTTTCCTAGATCTCT GCTTCACCACCAGTTCTATCCCCCAGCTGCTTTCAATCTAGGCAGCCAGGCAAGA CTATCAGCCACACGGGCTGTGCCATCCATCCAGCTCTTCATGTTCCTGGGCCTGGGTGGCA AGAGTGTATTCTCTTGGCAGCCGTGGCCTATGACCGCTTCATTGCAATCTGCAAGCC CCTTCACTATTCTGTCATTATGCACCCTCAGCTGTGCTGGAAGTTGGTGTCTGTGGC CCGGGGGTGTTGGACTCCTCAGTTCTCTAGTTATGTCTCCTGTGACTATGAAGCTGC CACGATGTGGAAGATGTAAGTTGAAACATTTCCTGTGTGAGATGCCAGCTCTAATA AAAATCACCTGTGTGGACACAGTGGCTATGGAGAGCACTGTTTCACCTTATCGGTA GTAATTGTCCTGATGCCTTTGTGTCTTATCCTCATCTCTTATAGCTACACTTGCCCCTAG CAGTGCTGAGAATCAAGTCAGCCACAGGAAGAAGGCCTTCAATATGTGCGGG TCCCACCTCACCGTGGTCGTCCTGTTTTATGGGAATATTATCTATATGTATATGCAA CCATGGAATAATTCTTCTCAGGACCAAGGGAAGTTCCTTACCCTTTTCTACAACTTA ATGACCCCCCATGTTAAACCCTGTCATCTATACACTGAGAAACAAGGATGTAAAAGG TGCACTGAAGAGGCTTGTGTCTAGAAAACACACTGACTGCTCTTGAGACT GCTTCTTTACTTATTTAATAGAAATAAATAATTCTTGAA	MPLSCPTRAAQKQFILLGFS GRPRLEHVLFVFVLIFYLVT LVGNIIILISHLDPCLHMPM YFFLTNLSFLDLCFTTSSIPQ LLFNLGSPGKTISHTGCAIQL FMFLGLGGKSVFSWQPWP MTASLQSASPFTILSLCTLSC AGSWCLWPGGVGLLSSLV MSPVTMKLPRCGRCKLKHF LCEMPALIKITCVDTVAMES TVFTLSVIVLMPLCLILISY SYIALAVLRIKSATGRRKAF NMCGSHLTVVSLFYGNIIY MYMQPWNNSSQDQGKFLT LFYNLMTPMLNPVIYTLRN KDVKGALKRLVSRKHSDSD CS

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC008745_A	109/110	TTGGCTGGACCAATGGGATGGAGAGAATCACTCAGTGGTATCTGAGTTTTGTTTCTG GGACTCACTCATTCATGGGAGGAGATCCAGCTCCTCCTCCTAGTGTTTTCCTCTGTGCTCT ATGTGGCAAGCATTACTGGAAACATCCTCATTGTGTTTCTGTGACCACTGACCCTC ACTTACACTCCCCATGTACTTTCTACTGGTCAGTCTCCTCCTTCATTGACTTAGGAGC CTGCTCTGTCACTTCTCCCAAGATGATTTATGACCTGTTCAGAAAGCGCAAAGTCAT CTCCTTTGGAGGCTGCATCGCTCAAATCTTCTTCATCCACGTCATTGGTGGTGTGGA GATGGTGCTGCTCATAGCCATTGAGCCCAAGAATGTGCCTTTCATTTCTGGCGTGTTGCCTG CCACTATCTGACCATTATGAGCCCAAGAATGTGCCAACTGGCATTTCTTGTTAATTTACCCTTC GACCCTTGTTGTCAGTCACTCCCGTTCCAACTGGCCTTCCTGACCTTCTCAGCTA TGTGGCCCTAATGTGTTGGACAGCTTCATGGCAGTCAGTGAACAGTGGTTTATC GCCTGTACCGACACCTACAGATTGCAGTTCATGCGACGTCTTAACTCCTGTTTACTGTTT TGTGTGGGTACTTTCTTCATACTTCTAATCTCCTAGCGTCTTCATCCTGTTTACTGTTT GGAAACATTCCTCAGGTGGTTCATCCAAGGCCCTTTCCACTCTTTCCAGCTCACAGCA CAGCGGTCCTTTTGTTCTTTGGTCCACCCATGTTTGTGTATACATGGCCACACCCTA ATTCACAGATGGACAAGTTTCTGGCTATTTTTGATGCAGTTCTCACTCCTTTTCTGA ATCCAGTTGTCTATACATTCAGGAATAACGAGGATCTCATAAAGATACAATAAGCCCTTCT C	MDGENHSVVSEFLFLGLTH SWEIQLLLVFSSVLYVASIT GNILIVFSVTTDPHLHSPMY FLLVSLSFIDLGACSVTSPK MIYDLFRKRKVISFGGCIAQI FFIHVIGGVEMVLLIAMAFD SYVALLKPLHYLTIMSPRM CLSFLAVAWTLVVSHSLFQ LAFLVNLPFCGPNVLDSFYC DLPQLLRLACTDTYRLQFM VTVNSGFICVGTFFILLISYV FILFTVWKHSSGGSSKALST LSAHSTAVLLFFGPPMFVYT WPHPNSQMDKFLAIFDAVL TPFLNPVVYTFRNKEMKAA IKRVCKQLVIYKKIS

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC016626_A	111/112	TTGGCTGGACCAATGGATGGAGAGAATCACTCAGTGGTATCTGAGTTTTGTTTCTGGGACTCACTCATTCATGGGGAGATCCAGCTCCTCCCTCCTAGTGTTTCCTCTGTGCTCTATGTGGCAAGCATTACTGGAAACATCCTCATTGTGTTTCTGTGACCACTGACCCTCACTTACACTCCCCCATGTACTTTCTACTGGTCAGTCTCTCCTTCATTGACTTAGGAGCCTGCTCTGTCACTTCTCCCAAGATGATTTATGACCTGTTCAGAAAGCGCAAAGTCATCTCCTTTGGAGGCTGCATCGCTCAAATCTTCTTCATCCACGTCATTGGTGGTGTGGAGATGGTGCTGCTCATAGCCATGGCCTTTGACAGTTATGTGGCCCTATTAAAGCCCCTCCACTATCTGACCATTATGAGCCCAAGAATGTGCCTTTCATTTCTGGCTGTTGCCTGGACCCTTGTTGTCAGTCACTCCCGTGTTCCAACTGGCATTTCTTGTTAATTTACCCTTCTGTGGCCCTAATGTGTTGGACAGCTTCTACTGTGACCTTCCTCAGCTTCTCAGACTAGCCTGTACCGACACCTACAGATTGCAGTTCATGGTCACTGTTAACAGTGGGTTTATCTGTGTGGGTACTTTCTTCTTATACTTCTAATCTCCTACGTCTTCATCCTGTTTACTGTTTGGAAACATTCCTCAGGTGGTTCATCCAAGGCCCTTTCCACTCTTTCAGCTCACAGCACAGCGGTCCTTTTGTTCTTTGGTCCACCCATGTTTGTGTATACATGGCCACACCCTAATTCACAGATGGACAAGTTTCTGGCTATTTTGATGCAGTTCCAGTTGTCACTCTTTCTGAATCCAGTTGTCTATACATTCAGGAATAAAGGAGATGAAGGCAGCAATAAAGAGAGTATGCAAACAGCTAGTGATTTACAAGAAGATCTCATAAATGATACAATAAGCCCTTCTC	MDGENHSVVSEFLFLGLTHSWEIQLLLLVFSSVLYVASITGNILIVFSVTTDPHLHSPMYFLLVSLSFIDLGACSVTSPKMIYDLFRKRKVISFGGCIAQIFFIHVIGGVEMVLLIAMAFDSYVALLKPLHYLTIMSPRMCLSFLAVAWTLVVSHSLFQLAFLVNLPFCGPNVLDSFYCDLPQLLRLACTDTYRLQFMVTVNSGFICVGTFFILLISYVFILFTVWKHSSGGSSKALSTLSAHSTAVLLFFGPPMFVYTWPHPNSQMDKFLAIFDAVLTPFLNPVVYTFRNKEMKAAIKRVCKQLVIYKKIS

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC002555_B	113/114	ACCAATGACATGGAGTGGGGCGGAACCATAGTGGGAGAGTGGGTGAGTTTGTGTTGCT GGGGCTTCCCTGCTCCTGCGCCACTACAGGTACTATTGTTTGCCCTTTTGCTGCTGG CCTATGTGTTGGTGCTGACTGAGAACACACTCATCATTATGGCAATTAGGAACCATT CCACCCTCCACAAACCCATGTACTTTTTCTAGCTAATATGTCCTTTCTGGAGATCTG GTATGTCACTGTCACTATTCCCAAGATGCTTGCTGGCTTTGTTGGATCCAAACAGGA TCATGGACAGCTAATCTCCTTGAGGGATGCATGACACAGCTCACTTTTTCCTTGG CTTGGGCTGCACTGAGTGTGTCCTTCTCGCTGTTATGGCCTATGATGGCTATATGGC CATCTGCTATCCTCCTCCACTACCCAGTCATTGTCAGTGGCCGGCTGTGTGTGCAGAT GGCTGCTGGCTCTTGGGCTGGAGGTTTTGGCATCTCCATGGTCAAAGTTTTTCTTAT TTCTGGCCTCTCTTACTGTGGCCCCAACATCATCAACCACTTTTTCTGTGATGTCTCT CCATTGCTCAACCTCTCATGCACTGATATGTCCACAGCAGCTTACAGATTTCATC CTGGCCATTTTTATTCTTCTAGGGCCACTCTCTGTCACTGGGCGCCTCCTATGTGGCC ATTACTGGTGCTGTGATGCACATTCCTTCGGCTGCTGGACGCTATAAGGCCTTTTCC ACCTGTGCCTCTCATCTCACTGTTGTGATAATCTTCTATGCAGCCAGTATCTTCATCT ATGCTCGGCCAAAGGCACTCTCAGCTTTTGACACCAACAAGTTGTCTCTGTACTGTA TGCTGTCATTGTACCATTGCTCAATCCCATCATTTACTGCCTGCGCAATCAAGAGGT CAAGAGAGCCCTATGCTGTACTCTGCACCCTGTACCAGCACCAGGATCCTGACCCCA AGAAAGCTAGCAGCAGAAATGTATAGAAGGGAT	MTWSGGTIVGEWVSLCCW GFPAPAPLQVLLFALLLAY VLVLTENTLIMAIRNHSTL HKPMYFFLANMSFLEIWYV TVTIPKMLAGFVGSKQDHG QLISFEGCMTQLYFFLGLGC TECVLLAVMAYDRYMAICY PLHYPVIVSGRLCVQMAAG SWAGGFGISMVKVFLISGLS YCGPNIINHFFCDVSPLLNLS CTDMSTAELTDFILAIFILLG PLSVTGASYVAITGAVMHIP SAAGRYKAFSTCASHLTVVI IFYAASIFIYARPKALSAFDT NKLSLYCMLSLYHCSIPSFT ACAIKRSREPYAVLCTLYQH QDPDPKKASRNV

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC002555_A	115/116	AATGATGTGGGAAAACTGGACAATTGTCAGTGAATTTGTTCTCGTGAGCTTCTCAGCCCTGTCCACTGAGCTTCAGGCTTCACTGTTTCTCCTTTTCTTGACCATTTACTTGGTTACTTTAATGGGCAATGTCCTCATCATCCTGGTCACTATAGCTGACTCTGCACTACAAAGTCCTATGTACTTCTTCCTCCAGAAACTTGTCCTTCCTGGAGATAGGTTTCAACTTGGTCATTGTGCCCAAGATGCTGGGGACCCTGATCATTCAAGACACAACCATCTCCTTCCTTGGATGTGCCACTCAGATGTATTTCTTTCTTTTTGGGGCTGCTGAGTGCTGCCCTTGGATGTGCCACTCAGATGTATTTCTTTCTTTTTGGGGCTGCTGAGTGCTGCCTCCTGGCCACCATGGCATATGACCGCTACGTGGCCATCTGTGACCCCTTGCACTACCCAGTCATCATGGGCCACATATCCTGTGCCCAGCTGGCAGCTGCCTCTTGGTTCTCAGGGTTTTCAGTGGCCACTGTGCAAACCACATGGATTTTCAGTTTCCCTTTTGTGGCCCCAACAGGGTGAACCACTTCTTCTGTGACAGCCCTCCTGTTATTGCACTGGTCTGTGCTGACACCTGTGTGTTGAACTGGAGGCTCTGACAGCCACTGTCCCATTCATTCTCTTTCCTTTCTTGCTGATCCTGGGATCCTATGTCCGCATCCTCTCCACTATCTTCAGGATGCCGTCAGCTGAGGGAAACATCAGGCATTCTCCCACCTGTTCCGCCCACCTCTTGGTTGTCTCTCTTCTATAGCACTGCCATCCTCAGCGTATTTCCACAGTGGTGACTCCCATGTTGTCTTCTCTGAGAGCAAGAAGTCTGTGTCTACTCACTTCTCAAGGAATAAAGAAGTGAAGGCTGCACTGAAGCGGCTAACCCCATCATCTACAGCCCTGGGCTCTCAGAAACTATGATTGGCTTAGATGGAAACTGAAGG	MMWENWTIVSEFVLVSFSALSTELQALLFLLFLTIYLVTLMGNVLIILVTIADSALQSPMYFFLRNLSFLEIGFNLVIVPKMLGTLIIQDTTISFLGCATQMYFFFFGAAECCLLATMAYDRYVAICDPLHYPVIMGHISCAQLAAASWFSGFSVATVQTTWIFSFPFCGPNRVNHFFCDSPPVIALVCADTSVFELEALTATVPFILFPFLLILGSYVRILSTIFRMPSAEGKHQAFSTCSAHLLVVSLFYSTAILTYFRPQSSASSESKKLLSLSSTVVTPMLNPIIYSSRNKEVKAALKRLIHRTLGSQKL

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC005255_A	117/118	ATGAAACCAGGGAATGATACACGAATTTCAGAATTTCTTCTTCTAGGACTTTCAGCAGAACCAGAATTGCAGCCCTTCTTCTTTGGGCTGTTCCTGTCCATGTACCTGGTCACCGTGCTCGGGAACCTGCTCATCATCCTGGCCACAATCTCAGACTCCCACCTCCACACCCCCATGTACTTCTTCTCCTCCAACCTGTCCTTTGCAGATATCAGTTTTGTGTCTACCACTGTCCCGAAGATGCTGGTGAATATCCAGACGCAGAGCAGGGTCATCACCTATGCAGGCTGCATCACCCAGATGTGCTTTTTCCTACTATTTGCAGTGTTGGACAGCCTTCTCCTAGCTGTGATGGCCTATGACCGGTTTGTGGCCATCTGTCATCCTCTGTACTACACAATCATCATGAACCCTCAGTTCTATAGATGGATTCTTAGTGTCCTGAATTCTCTGTTACAAAGCTTAATGGTGTTGCCACTGCCCTTCTATACAGACATAGCAATCCCCCACTTTTTCTGTGAACTTAATCAGATAATCTGCATTGCCTGTTCTGACACCTTTCTTAATGACATCATGATATATTGTGCAACTGTGCTGCTGGGCGGTCCCCTGACTGGAATCCTTTACTCTTACTCTAAGATAGTTTCCTCCATACGTGCAATCTCAGCTCAGGGGAAGTACAAGGCATTTTCCACCTGTGCATCTCACCTCAGTTGTCTCCTTGTTTTATGGTACAAGCCTAGGAATGTACCTTAGTTCTGCTGCAACCCACACTCACCCTCAAGTGCAACAGCCTCAGTGATGATGTACACTGTGGTCACCCCATGCTGAACCCTTTATCTACAGTCTGAGGAATAAAGACCTAAAGGATGCTCTGAAACGCTTCTTCAGAAGGAAGCAATAAAAGGACTCTTCTTCAATTAATGCCT	MKPGNDTRISEFLLLGLSAEPELQPFFGLFLSMYLVTVLGNLLILATISDSHLHTPMYFFLSNLSFADISFVSTTVPKMLVNIQTQSRVITYAGCITQMCFFLLFAVLDSLLLAVMAYDRFVAICHPLYYTIIMNPQFYRWILSVLNSLLQSLMVLPLPFYTDIAIPHFFCELNQIICIACSDTFLNDIMIYCATVLLGGGPLTGILYSYSKIVSSIRAISSAQGKYKAFSTCASHLSVVSLFYGTSLGMYLSSAATHNSPSSATASVMYTVVTPMLNPFIYSLRNKDLKDALKRFFRRKQ

Table 1

Acc. No.	SEQ ID NO (Nucl)/ SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC002988_A	119/120	ATGAAAGCAGGGAATGAGACACAAATTTCAGAATTTCTTCTTCTTCTAGGATTTTCAGA GAAACAAGAATTGCAGCCCTTCCTCTTTGGGCTGTGTTCCTGTCCATGTACCTGGTCAC TGTGCTCGGGAACCTGCTCATCATCCTGGCCGCAATCTCAGACTCCTGCCTCCACAC CCCCATGTACTTCTTTCTCTCCAACCTGTCCTTCGTAGATATCTGTTTTGCCTCCACC ATGGTCCCAAAGATGTTGGTGAACATCCAGACACAGAGCAAAGTCATTACCTATGC AGGTTGCATCACCCAGATGTGCTTTTTTGTACTCTTTATAGTGTTGGACAGCTTACT CCTGACCGTGATGGCCTATGACCAGTTGTGGCCATCTGTCACCCCCTGCCACTACAC GGTCATCATGAGCCCTCAGCTCGTGTGGACTCGTGGTTCTGGTGTCCTGGATCATGAG TGTCCTAAACTCCATGTTACAAAGCTTAGTGACATTGACAGTTGTCCTTCTGCACAGA CTTGGAAATCCCTCACTTTTCTGTGAACTAATGAGATGATCCACCTTGCCTGTTCT GACACCTTTGTGAACAACATGGTGATGCATTTGCAGCTGTGCTGGACGGTGG TCCTCTCGTTGGGATCCTTTATTCTTACTGTAGGATAGTTCCTCCATACGTGCAATC TCGTCAACTCAGGGGAAGTACAAGGCACTTCCACCTGTCATCTCACCTCTCAGTT GTCTCCATATTTTATGGTACGGGGCTAGGGGTGTACCTTAGCTCTACTATGACCAA AACTTACACTCAACTGCTGTCGCCTCGGTGATGTACACTGTGGTCACCCCCATGCTC AACCCCTTCATTTACAGTCTGAGGAATAAAGACATAAAGGGGGCTCTGACACAATT CTTCAGAGGGAAACAATAAAAAGAGCCATTTTTCGGCTGGGCACA	MKAGNETQISEFLLLGFSEK QELQPFLFGLFLSMYLVTVL GNLLILAAISDSCLHTPMYF FLSNLSFVDICFASTMVPKM LVNIQTQSKVITYAGCITQM CFFVLFIVLDSLLLTVMAYD QFVAICHPLHYTVIMSPQLC GLLVLVSWIMSVLNSMLQS LVTLQLSFCTDLEIPHFFCEL NEMIHLACSDTFVNNMVM HFAAVLLDGGPLVGILYSYC RIVSSIRAISSTQGKYKALST CASHLSVVSIFYGTGLGVYL SSTMTQNLHSTAVASVMYT VVTPMLNPFIYSLRNKDIKG ALTQFFRGKQ

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Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC006271_B	121/122	CTCTGACTCCCACCTCCCACACCCCCATGTACTTCTTCCTCTCTCCAACCTGTCCTTGGCT GACATCGGTTCACCTCCACCACGGTCCCCAAGATGATTGTGGACATGCAAACTCAC AGCAGAGTCATCTCCTATGAAGGCTGCCTGACTCAGATGTCTTTTTTTGTCCTTTTT GCATGTATGGATGACATGCTCCTGAGTGTGATGGCCTATGACCGGTTGTGGCCATC TGTCACCCCCTGCACTACCGAATCATCATGAACCCACGCCTCTGTGGCTTCTTAATC TTGTTGTCTTTTTTTTATTAGTCTTTTGGACTCCCAGTTGCACAATTTGATTATGTTAC AGCTCACCTGCTTCAAGGATGTGGACATTTCTAATTTCTTCTGTGACCCTTCTCAAC TCCTCCACCTTAGGTGTTCCGACACCTTCATCAATGAAATGGTCATATTTCATGG GTGCCATATTTGGCTGTCTCCCTATCTCAGGGATCCTTTCTTCTTACTATAAAATTGT TTCCCCCATTCTGAGAGTTCCAACATCAGATGGGAAGTATAAAGCCTTCCCACCTG TGGCTCTCACCTGGCAGTTGTTTGCTTATTTTATGGAACAGGGCTTGTAGGGTACCT CAGTTCAGCTGGTGTTACCATCCCCAGGAAGAGTATGGTGGCTTCAGTGATGTACAC TGTGGTCACCCCCATGCTGAACCCCTTCATCTACAGCCTGAGGAACAAGGACATTCA AAGTGCCCTGTGCAGGCTGCATGGCAGAATCATCAAATCTCAAATCTCCATCCTTT TTGTTATATGGGATAGAAATGGCAGCAAAATTTAACACCTAGGCCTGCAAATTCTG CCTCCTTG	MYFFLSNLSLADIGFTSTTV PKMIVDMQTHSRVISYEGC LTQMSFFVLFACMDDMLLS VMAYDRFVAICHPLHYRIIM NPRLCGFLILLSFFISLLDSQL HNLIMLQLTCFKDVDISNFF CDPSQLHLRCSDTFINEMV IYFMGAIFGCLPISGILFSYY KIVSPILRVPTSDGKYKAFS TCGSHLAVVCLFYGTGLVG YLSSAVLPSPRKSMVASVM YTVVTPMLNPFIYSLRNKDI QSALCRLHGRIIKSHHLHPF CYMG

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC023080_A	123/124	ACCAAAATTATTTTATTGTTCAAAAATGTATGTTCAAAATTGCAATCCTTGTGTCTATT CACAGAAAAATCAATTATCCAAATACCAAACTGGATTTCGAGCAAGTGAACAACAT AACGGAATTCATCTTGCTTGGCCTGACACAGAACGCAGAGGCACAGAAACTCTTGT TTGCTGTGTTTACACTCATCTACTTTCTCACCATGGTAGACAACCTAATCATTGTGG TGACAATCACCACCAGCCCAGCCCTGGACTCCCCGTGTATTTTTCTGTCTTTCTT TTCCTTCATAGATGGCTGCTCCTCTTCTACCATGGCCCCAAAATGATATTTGACTT ACTCACTGAAAAGAAAACTATTTCCTTCAGTGGGTGCATGACCCAGCTCTTTGTAGA ACATTTCTTTGGGGGAGTTGAGATCATTCTGCTCGTGGTGATGGCCTATGACTGCTA TGTGGCCATCTGCAAGCCCCTGTACTACCTGATCACAATGAACAGGCAGGTATGTG GCCTCCTGGTGGCCATGGCATGGGTCGGGGGATTTCTTCACGCTCTGATTCAAATGC TTTTAATAGTCTGGCTGCCCTTCTGTGGCCCAATGTCATTGACCATTCATCTGTG ACCTTTCCCTGCTGCTAAAACTCTCCTGCACTGACACTCACGTCTTTGGACTCTTTGT TGCCGCCAACAGTGGGCTGATGTGTATGCTCATTTTTCTATTCTTATTACCTCTTAC GTCCTAATCCTCTGCTCACAGCGGAAGGCTCTCTCTACCTGCGCCTTCCATATCACT GTAGTCGTCTATTCTTTGTTCCCTGTATATTGGTACGCTTCGACCATGATCACCT TCCCTATTGATAAAGCTGTGTCTGTGTTTTATACTGGTGGTAACACCCATGTTAAACC CTTTAATCTACACCCTCAGAAACACAGAGGTGAAAAATGCCATGAAGCAGCTCTGG AGCCAAATAAATCTGGGGTAACAATTTGTGTGATTAGAGAAGATAAACACAGAACCT ACTCATATTTTAACAACAG	MYVSNCNPCAIHRKINYPN TKLDFEQVNNTEFILLGLT QNAEAQKLLFAVFTLIYFLT MVDNLIIVTITTSPALDSPV YFFLSFFSFIDGCSSSTMAPK MIFDLLTEKKTISFSGCMTQ LFVEHFFGGVEIILLVVMAY DCYVAICKPLYYLITMNRQ VCGLLVAMAWVGGFLHALI QMLLIVWLPFCGPNVIDHFI CDLFPLLKLSCTDTHVFGLF VAANSGLMCMLIFSILITSY VLILCSQRKALSTCAFHITV VVLFFVPCILVYLRPMITFPI DKAVSVFYTVVTPMLNPLI YTLRNTEVKNAMKQLWSQI IWGNNLCD

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022891_A	125/126	CCATATAAATGGCTGACAGAAATGTCACTGTGATAACTGAATTCATCCTCCTGGGGT TGACTGATAACCCTGAAATGAATGTTGTCCTTTCGTGCTCTTTCTATTAATCTATCT CATTACTGTCTTGGGCAACTTTTGGATTATCATAATAATTCTGGCTAGTGCCCAACT CCATTCACCCATGTACTTTTTCCTTAGCCAGTTGGCTTTCTTAGATTTCTGCTATTCT TCAGTCTTGATTCCTAAAAATGTTGGTGAATTACATAGCAGGACAGAAAGTCATCTCT TATCACGGTTGCCTCCTTCAGTATTCCTTTGTCAGCGTTGTTCCTGACTACTGAAATGCT TCCTCCTGGCTGCTGCCATGGCATGTGATCGTATCGCTGTTTGCCACCCACTTCACT ACAAAGGTCTCATGACTCCTACTTTCTGGATCTATTTGGTGACTGTTTCTTACCTGCT GGGCTCTGTAAACTCCCTCACCCACCTGAGTAGCTTACTCAGTTTGTCTTTCTGTGG GTCCAATGTTATCAACCGTATTTCTGTGACATTCCATTGCTCCTTCCAACTCTCCTGT TCCAACACCCAACACAGTAAGATTTTATTTACTGCGTCCTTCTGGAGCAACATCAGTG ACTACCTTTTTGATAGTGGTTAGTTCCTATCTGGTAATCCTACTCATTGTCCTGAAG ATACATTCCACCAGGGGCAGAAATAAAGCCATATCCACATGTGCCTCCCACCTAAT GGTAGTGACTCTCTTCTTACAGAACCAGTGATATTTACTTATCTGGGAGCCAACCCTGG ATACTCACAGGATAGACCCAAAATTCTGCCTGTGGAGTGCACACTTTTGTTGTCAAT ACTAAATCTTCTAATATATAGGCGTGAGAAACAGAGAAGTCAAAGAAGCCATAAAAA TAATTATTAAGAGAAAAAATACTTCCCTCAGTGAACATGAATTTTCAGCCAGAAACATT TAAGACTATTATCA	MADRNVTVITEFILLGLTDN PEMNVVLSVLFLLIYLITVL GNFWIIIILASAQLHSPMYF FLSQLAFLDFCYSSVLIPKM LVNYIAGQKVISYHGCLLQ YSFVSLFLTECFLLAAMAC DRYLAVCHPLHYKGLMTPT FWIYLVTVSYLLGSVNSLTH LSSLLSLSFCGSNVINRYFCD IPLLFQLSCSNTQHSKILFTV LSGATSVTTFLIVVSSYLVIL LIVLKIHSTRGRNKAISTCAS HLMVVTLFYRTVIFTYLGA NPGYSQDRPKILPVECTLLL SILNLLIYSVRNREVKEAIKII IKRKILPQ

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022289_B	127/128	GATCAACTTTCTTATGTTTTCTCACAGGATTCAAAAAAATCAGACTGCTGGAGTCAC CTTCATCCTCTTGGGCTTCTCAGAATTTCCAGACCTTCAGATACCCCTGTTCCTGGTC TTCCTGACCATCTACACAATCACTGTGATGGGAATCTGGGCATGATCATGGTCATC AGGATCAACCCCAAACTCCACACCCCTATGTACTTTTTCCTCAGCCACTTGTCCTTT GTTGATTTCTGTTATTCCACCACAATTACACCAAAACTGCTGGAGAACTTGGTTGTG GAAGACAGAATCATCTCCTTCACAGGATGCATCATGCAATTCTTCTTTGCCTGTATA TTTGTGGTGACAGAAAACATTCATGCTGGCAGCGATGGCTTATGACAGATTTGTGGC AGTGGTGTAACCCTCTGCTTTACACAGTTGCAATGTCCCAGAGGCTTTGCTCCTTGTT AGTGGCTGCATCATACTCTTGGAGTTTAGTTTGTTGTTCCTTAACATACACATATTTCT GTTGACTTTATCTTTTGTGTAGGACTAACTTCATTAATAACTTTGTCTGTGAGCACGCT GCCATTGTTGCTGTGTCCTCGCTCTGACCCCTACATGAGCCAGAAGGTCATTTTAGTT TCTGCAACATTCAATGAAATAAGCAGCCTGGTGATCATTCTCACTTCCTATGCTTTC ATTTTTATCACTGTCATGAAGATGCCTTCCACTGGGGGCGCAAGAAAGCGTTCTCC ACGTGTGCCTCCCACCTGACCGCCATTACCATTTTCCATGGGACTATCCTTTTTCTCT ACTGTGTTCCTAACTCCAAAAGTTCATGGCTCATGGTCAAGGTGGCCTCTGCTCTTTT ACACAGTGGTCATTCCCATGCTGAACCCCTTGATCTATAGCCTCAGGAACAAAGAT GTAAAAGAGACAGTCAGGAAGTTAGTCATTACCAAATTATTATGTCATAAAAATGTA ATGCTAGAAATATTAATTATTTATCCTTGAGAGCAGCACTGCA	MFSHRIQKNQTAGVTFILLG FSEFPDLQIPLFLVFLTIYTIT VMGNLGMIMVIRINPKLHT PMYFFLSHLSFVDFCYSTTI TPKLLENLVVEDRIISFTGCI MQFFFACIFVVTETFMLAA MAYDRFVAVCNPLLYTVA MSQRLCSLLVAASYSWSLV CSLTYTYFLLTLSFCRTNFIN NFVCEHAAIVAVSCSDPYM SQKVILVSATFNEISSLVIILT SYAFIFITVMKMPSTGGRKK AFSTCASHLTAITIFHGTILF LYCVPNSKSSWLMVKVASV FYTVVIPMLNPLIYSLRNKD VKETVRKLVITKLLCHKM

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC022289_A	129/130	CGATGCTGCTGACAGATAGAAATACAAGTGGGACCACGTTCACCCTCTTGGGCTTC TCAGATTACCCAGAACTGCAAGTCCCACTCTTCCTGGTTTTCTGGCCATCTACAAT GTCACTGTGCTAGGGAATATTGGGTTGATTGTGATCATCAAAATCAACCCCAAACT GCATACCCCCATGTACTTTTTCCTCAGCCAACTCTCCTTTGTGGATTTCTGCTATTCC TCCATCATTGCTCCCAAGATGTTGGTGAACCTTGTGTCAAAGACAGAACCATTTCA TTTTTAGGATGCGTAGTACAATTCTTTTTCTTCTGTACCTTTGTGGTCACTGAATCCT TTTTATTAGCTGTGATGGCCTATGACCGCTTCGTGGCCATTTGCAACCCTCTGCTCT ACACAGTTGACATGTCCCAGAAACTCTGCGTGTTGGGATCCTATGCCT GGGGAGTCTCATGTTCCTTGGAACTGACGTGCTCTGCTTTAAAGTTATGTTTTCATG GTTTCAACACAATCAATCACTTCTTCTGTAGTTCTCCTCACTACTCTCCCTTTCTTG CTCTGATACTTACATCAACCAGTGGCTCATTCTTTCTTGCCACCTTAATGAAAT CAGCACACTACTCATCGTTCTCACATCTTATGCGTTCATTGTTAACCATCCTCAA GATGCGTTCAGTCAGTGGGCGGCCGCAAAGCCTTCTCCACCTGCCTCCCACCTGAC TGCCATCACCATCTTCCATGGCACCATCCTTCCTTACTGTGTGCCCAACTCCAAA AACTCCAGGCACCACAGTCAAAGTGGCCTCTGAGAAATAAAGATGTCAAGGATACCAGTCACCGA TTGAATCCCCTGATCTACAGTCTGAGAAATAAAGATGTCAAGGATACCAGTCACCGA GATACTGGACACCCAAAGTCTTCTCTTACTGAGCCT	MLLTDRNTSGTTFTLLGFSD YPELQVPLFLVFLAIYNVTV LGNIGLIVIKINPKLHTPMY FFLSQLSFVDFCYSSIIAPKM LVNLVVKDRTISFLGCVVQF FFFCTFVVTESFLLAVMAYD RFVAICNPLLYTVDMSQKL CVLLVVGSYAWGVSCSLEL TCSALKLCFHGFNTINHFFC EFSSLLSLSCSDTYINQWLLF FLATFNEISTLLIVLTSYAFIV VTILKMRSVSGRRKAFSTCA SHLTAITIFHGTILFLYCVPN SKNSRHTVKVASVFYTVVIP MLNPLIYSLRNKDVKDTVT EILDTKVFSY

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC009594_C	131/132	AACACACATGGAGACAAGAAATTACTCTGCCATGACTGAATTCTTTCTGGTGGGGCTTT CCCAATATCCAGAGCTCCAGCTTTTTCTGTTCCTGCTCTGCCTCATCATGTACATGAT AATCCCTCGGGAAATAGCCTCCTCCTCATTATCATCACCATCTTGGATTCTCGCCTCCA TACTCCCATGTATTTCTTTCTTGGAAACCTCTCATTCTTGGACATCTGTTACACATCC TCATCCATTCCTCCAATGCTTATTATTTATTTATGTCTGAGAGAAAATCCATCTCCTTCA TTGGCTGTCTGTGCCTGCAGATGGTTGTGTCCCTTGGGCTCCACTGAGTGTGTCC TCCTGGCTGTGATGGCCTATGACCACTATGTGGCCATCTGCAACCCACTGAGGTACT CCATCATCATGAACGGAGTGCTGTATGTGCAAATGGCTGCAAATGGTCCTGGATCATA GGCTGTCTGACCTCCCTATTGCAAACAGTTCTGACAATGATGTTGCCTTTCTGTGGG AATAAGTCATTGATCATATTACCTGTGAAATTTGGCCCTTCTAAAACTTGTTTGT TCAGATATCACCATCAATGTGCTTATCATGACAGTGACAAATATTGTTTCACTGGTG ATTCTTCTACTGTTAATTTCATCTCCTATGTGTTTATTCTCTCTTCCATCCTGAGAA TTAATTGTGCTGAGGGAAGAAAAGAAAGCCTTCTCTACCTGTTCAGCGCACTCGATTG TGGTCATCTTATTCTACGGTTCAGCCGTTTTTATGTACATGAAACCCAAGTCAAAGA ACACTAATAACATCTGATGAGATTATTGGGCTGTCTTATGGAGTGGTAAGCCCAATGT TAAATCCCATCATCTATAGCCTCAGGAATAAAGAGGTCAAAGAGGCTGTAAAGAAA GTCCTGAGCAGCAGACATCTGCATTTATTGAAAAATGTGAAAAAAACCTTGGGCATGCGATA TCCTCAATGGGGCAAGAGA	METRNYSAMTEFFLVGLSQ YPELQLFLFLLCLIMYMIILL GNSLLIITILDSRLHTPMYFF LGNLSFLDICYTSSSIPPMLII FMSERKSISFIGCALQMVVS LGLGSTECVLLAVMAYDHY VAICNPLRYSIIMNGVLYVQ MAAWSWIIGCLTSLLQTVL TMMLPFCGNNVIDHITCEIL ALLKLVCSDITINVLIMTVT NIVSLVILLLIFISYVFILSSI LRINCAEGRKKAFSTCSAHS IVVILFYGSALFMYMKPKSK NTNTSDEIIGLSYGVVSPML NPIIYSLRNKEVKEAVKKVL SRHLHLLKM

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
CG50297_01	133/134	ACATGGAGACAAGAAATTACTCTGCCATGACTGACTGAATTCTTTCTGGTGGGGCTTTCCC AATATCCAGAGCTCCAGCTTTTTCTGTTCCTGCTCTGCCTCATCATGTACATGATAA TCCTCCTGGGAAATAGCCTCCTCATTATCATCACCATCTTGGATTCTCGCCTCCATA CTCCCATGTATTTCTTTCTTGGAAACCTCCATCTTTGGACATCTGTTACACATCCTC ATCCATTCCTCCAATGCTTATTATTATTTATGTCTGAGAGAAAATCCATCTCCTTCATT GGCTGCTGCTCTGCAGATGGTTGTGTCTCCCTTGGCTTGGGCTCCCACTGAGTGTCCTC CTGGCTGTGATGGCCTATGACCACTATGTGGCCATCTGCAACCCACTGAGGTACTCC ATCATCATGAACGGAGTGCTGTATGTGCAAATGGCTGCATGGTCCTGGATCATAGG CTGTCTGACCTCCCTATTGCACACAGTTCTGACAATGATGTTGCCTTTCTGTGGGAA TAATGTCATTGATCATATTACCTGTGAAATTTTGGCCCCTTCTAAAACTTGTTTGTTCA GATATCACCACCATCAATGTGCTTATCATGACAGTGACAAATATTGTTTCACTGGTGATT CTTCTACTGTTAATTTCATCTCCTATGTGTTATTCTCTCTTCCATCCTGTTCAGCGCACTCGATTGTG ATTGTGCTGAGGGAAGAAAGAAAGCCTTCTCTACCTGTTCAGCGCACTCGATTGTG GTCATCTTATTCTACGGTTCAGCCCTTTTTATGTACATGAAAACCCAAGTCAAAGAAC ACTAATACATCTGATGAGATTATTGGGCTGTCTTATGGAGTGGTAAGCCCAATGTTA AATCCCCATCATCTATAGCCTCAGGAATAAAGAGGTCAAAGAAGGCTGTAAAGAAAGT CCTGAGCAGAGACATCTGCATTTATTGAAAATGTGAAAAACCTTGGGCATGCGATATC CTCAATGGGGCAAGAGAGCTT	METRNYSAMTEFFLVGLSQ YPELQLFLLCLIMYMILL GNSLLIITILDSRLHTPMYFF LGNLSFLDICYTSSSIPPMLII FMSERKSISFIGCALQMVVS LGLGSTECVLLAVMAYDHY VAICNPLRYSIIMNGVLYVQ MAAWSWIIGCLTSLLHTVL TMMLPFCGNNVIDHITCEIL ALLKLVCSDITINVLIMTVT NIVSLVILLLIFISYVFILSSI LRINCAEGRKKAFSTCSAHS IVVILFYGSALFMYMKPKSK NTNTSDEIIGLSYGVVSPML NPIIYSLRNKEVKEAVKKVL SRHLHLLKM

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC009545_A	135/136	AACACCATGAAAAATAAGAACAATGTGACTGAATTTATCCTCTTAGGGCTCACACAG AACCCTGAGGGGCAAAAGGTTTTATTTGTCACATTCTTACTAATCTACACATGGTGACG ATAATGGGCAACCTGCTTATCATAGTGACCATCATGGCCAGCCAGTCCCTGGGTTCC CCCATGTACTTTTTTCTGGCTCTTCTTTATCATTCATAGATACCGTCTATTCTACTGCAT TTGCTCCCAAAATGATTGTTGACTTGCTCTCTGAGAAAAAGACCATTTCCTTTCAGG GTTGTATGGCTCAACTTTTTATGGATCATTTATTTGCTGGTGCTGAAGTCATTCTTCT GGTGGTAATGGCCTATGATCGATACATGGCCATCTGTAAGCCTCTTCATGAATTGAT CACCATGAATCGTCGAGTCTGTGTTCTTATGCTGTTGGCGGCCTGGATTGGAGGCTT TCTTCACTCATTGGTTCAATTTCTCTTTATTTATCAGCTCCCTTTCTGTGGACCCAAT GTCATTGACAACTTCCTGTGTGTATTGTATCCCTTATTGAAACTTGCTTGCACCAAT ACCTATGTCACTGGGCTTTCCTATGGGTCATATTACACTCTCTTAAGACTCAGAGTT TTCTTCACTATCCTGCTTTCCTATGGGTCATCATTACACCTGTCATCCCACGTCACTGTGGTCATTT TGGAAGGGAAACGAAAAGCTTTCTACACCTGTCATCCCACGTCACTGTGGTCATTT TATTCTTTGTCCCCTGTATCTTCTTGTATGCAAGGCCCAATTCTACTTTTCCCATTGA TAAATCCATGACTGACTGAGTTCTCAACTTTTATAACTCCCATGCTGAACCCACTAATCTA TACCCTGAAGAATGCAGAAATGCAGAAAGTGCCATGAGGAAACTTTGGAGTAAAAAAA GTAAGCTTAGCTGCGGGAAATGGCTGTATCACTCATGAGAAT	MKNKNNVTEFILLGLTQNP EGQKVLFVTFLLIYMVTIMG NLLIIVTIMASQSLGSPMYFF LASLSFIDTVYSTAFAPKMI VDLLSEKKTISFQGCMAQLF MDHLFAGAEVILLVVMAYD RYMAICKPLHELITMNRRV CVLMLLAAWIGGFLHSLVQ FLFIYQLPFCGPNVIDNFLCD LYPLLKLACTNTYVTGLSMI ANGGAICAVTFFTILLSYGVI LHSLKTQSLEGKRKAFYTC ASHVTVVILFFVPCIFLYARP NSTFPIDKSMTVVLTFITPM LNPLIYTLKNAEMKSAMRK LWSKKVSLAGKWLYHS

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC005962_B	137/138	AAAACACCATGGAAACACAGGGAACCTCACGTGGGTATCAGACTTTGTCTTCCTGGGG CTCTCGCAGACTCGGGAGCTCCAGCGTTCCTGTTTCTAAATGTTCCTGTTTGTCTAC ATCACCACTGTTATGGGAAACATCCTTATCATCATCACAGTGACCTCTGATTCCCAG CTCCACACACCCATGTACTTTCTGCTCCGAAACCTGGCTGTCCTAGACCTCTGTTTCT CTTCAGTCACTGCTCCCAAAATGCTAGTGGACCTCCTCTCTGAGAAGAAAACCATCT CTTACCAGGGCTGCATGGGTCAGATCTTCTTCTTCCCACTTTTGGGAGGTGCCATGG TCTTCTTCCTCTCAGTGATGGCCTTTGACCGCCTCATCTCCCGGCCCCTCCG CTATGTCACCGTCATGAACACTCAGCTCTGGGTGGGGCTCGTGGTAGCCACCTGGG TGGGAGGCTTTGTCCACTCTATTGTCCAGCTGGCTCTGATGCTCCCACTGCCCTTCT GTGGCCCCAACATTTGGATAACTTCTACTGTGTTCCCAAGTACTGAGACTTG CCTGCACTGACACCTCACTGCTGGAGTTCCTCAAGATCTCCAACAGTGGCGTGCTGG ATGTCGTCTGGTTCTTCCTCCTCCTGATGTCCTACTTATTCATCCTGGTGATGCTGAG GTCACATCCAGGGGAGGCAAGAAGGAAGGCAGCTTCCACCTGCACCACCCACATCA TCGTGGTTTCCATGATCTTCGTTCCAAGCATTTACCTCTATGCCCGGCCCTTCACTCC ATTCCCTATGGACAAGCTTGTGTCCATCGGCCACACAGTCATGACCCCATGCTCAA CCCCATGATCTATACCCTGAGGAACCAGGACATGCAGGCAGCAGTGAGAAGATTAG GGAGACACCGGCTGGTTTGAGA	METQNLTVTEFILLGLTQS QDAQLLVFVLVLIFYLILPG NFLIIFTIKSDPGLTAPLYFFL GNLALLDASYSFIVVPRMLV DFLSEKKVISYRSCITQLFFL HFLGAGEMFLLVVMAFDRY IAICRPLHYSTIMNPRACYA LSLVLWLGGFIHSIVQVALIL HLPFCGPNQLDNFFCDVPQ VIKLACTNTFVVELLMVSNS GLLSLLCFLGLLASYAVILC RIREHSSEGKSKAISTCTTHII IIFLMFGPAIFIYTCPFQAFPA DKVVSLFHTVIFPLMNPVIY TLRNQEVKASMRKLLSQH MFC

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL163152_C	139/140	GCCATGAAACTATTAAATCAATCTCAAGTGTCAGAATTCATTTTGCTGGGACTGACC AGCTCCCAGGATGTAGAGTTTCTTCTTCTTGCCCTCTTCTCGGTTATCTATGTGGTCA CAGTTTTGGGTAACCTTCTTATTATAGTCACAGTGTTAACACCCTAACCTGAATA CTCCCATGTATTTCTCCTGGTAATCTCTCTTTGTAGATATGACCCTTGCTTCTTT TGCCACCCCTAAGGTGATTCTGAACTTGTTAAAAAGCAGAAGGTAATTTCTTTTGC TGGGTGCTTCACTCAGATATTTCTCCTTCACTTACTGGGTGGGGTTGAAATGGTACT GTTGGTCTCCATGGCTTTTGACAGATATGTGGCCATTTGTAAGCCCCTACACTACAT GACCATCATGAACAAGAAGGTATGTGTTTTGCTTGTGAGTGACCTCATGGCTCTTGGG TCTCCTTCACTCAGGGTTCAGATACCATTTGCTGTGAACTTGCCCTTTTGTGGTCCC AATGTGGTAGACAGCAGCATTTTTGTGACCTCCCTTGGTACCTAAGCTTGCCTGTATA GACATATATTTGTACAGTAGTCATTGTTGCCAACAGTGGCATAATCTCCCTGAGC TGTTTCATTATTTTGCTTATCCTACAGTCCTCATAACCATTAAGAACCACT CTCCTACTGGGCAATCTAAAGCCCGTTCCACTTGACTGCTCACATCACAGTGGTGA TTCTCTTCTTTGGCCCATGCCATCTTTATCTACATTTGGCCCTTCGGCAACCACTCTGT AGATAAGTTCCTTGCTGTGTTTTATACCATCCATCACTCCTATCTTGAATCCAATTATC TATACTCTGAGAAACAAGAAGAAATGAAGATATCCATGAAAAAACTCTGGAGAGCTTT TGTGAATTCTAGAGAAGATACTTAGATTAAAAATATAATG	MKLLNQSQVSEFILLGLTSS QDVEFLLFALFSVIYVVTVL GNLLIIVTVFNTPNLNTPMY FLLGNLSFVDMTLASFATPK VILNLLKKQKVISFAGCFTQI FLLHLLGGVEMVLLVSMAF DRYVAICKPLHYMTIMNKK VCVLLVVTSWLLGLLHSGF QIPFAVNLPFCGPNVVDSIFC DLPLVTKLACIDIYFVQVVI VANSGIISLSCFIILLISYSLILI TIKNHSPTGQSKARSTLTAH ITVVILFFGPCIFIYIWPFGNH SVDKFLAVFYTITPILNPIIY TLRNKEMKISMKKLWRAFV NSREDT

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL359218_E	141/142	ATCAAATGGATAAAAACCAAACAGAAGTGATGAGAGAATTTTTCTTGTCAGGGTTC TCACAGACACCATCTATTGAAGCAGGGCTATTTGTACTATTTCTTTCTTCTATATGT CCATTTGGGTTGGCAATGTCCTCATCATGGTCACAGTAGCATCTGATAAATACCTGA ATTCATCACCCATGTATTTCCTTCTTGGCAACCTCTCATTTCTGGACCTATGTTATTC AACAGTAACGACCCCTAAGCTTCTGGCTGACTTCTTTAATCATGAAAAACTCATTTC CTATGACCAATGCATTGTGCAACTCTTCCTGCATTTTGTAGGGGCAGCTGAGAT GTTCCTGCTCACAGTGATGGCTACGATCGCTATGTTGCAATCTGTCGCCCGCTGCA CTACACCACTGTCATGAGTCGGGGGGTTATGCTGTGTGTTGGTTGCTGCCTCCTGGAT GGGAGGATTGTGCACTCCACTGGGAAAACTTTTTTTGTGATGTTCCCCCTGTCATCAACTTGC TGGGCCAAATCAGGTGGAAAACTTTTTTTGTGATGTTCCCCCTGTCATCAACTTGC TTGTGCTGACACTTTGTCATTGAATTGCTCATGGTATCATGGTATCTAACAGTGGGTTGATCTC CACCATCTCCTTGTGGTGCTGATTTCCTCCTACACCACTATCCTAGTCAAGATTCGC TCCAAGGAAGGAAGGCGAAAGGCCACTCTCCACGTGCCTCTCCACCTCATGGTGGT AACACTGTTTTTGGACCCTGTATTTCATCTACCGCTCGTCCTTTCTCTACATTTTCT GTGGACAAGATGGTGTCTGTACTCTACAATGTTATTACCCCAAATGCTAAACCCCTC ATCTACACACTTCGGAACAAAGAGGTAAAGTCAGCCATGCAGAAGAGCTCTGGGTCAG AAATGGGCTTACTTGGAAAAAGCAGGAGGAGACATTGAGACACATTGATATGAATTTTTGAA A	MDKNQTEVMREFFLSGFSQ TPSIEAGLFVLFLFFYMSIW VGNVLIMVTVASDKYLNSS PMYFLLGNLSFLDLCYSTVT TPKLLADFFNHEKLISYDQC IVQLFLHFVGAAEMFLLTV MAYDRYVAICRPLHYTTVM SRGLCCVLVAASWMGGFV HSTVQTILTVHLPFCGPNQV ENFFCDVPPVIKLACADTFV IELLMVSNSGLISTISFVVLIS SYTTILVKIRSKEGRRKALS TCASHLMVVTLFFGPCIFIY ARPFSTFSVDKMVSVLYNVI TPMLNPLIYTLRNKEVKSA MQKLWVRNGLTWKKQET

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Table 1

Acc. No.	SEQ ID NO (Nucl)/SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAI.163152_B	143/144	AGTAAATGAATCTTAAAAATGGATCTCTAGTGACCGAGTTTATTTTACTAGGATTTT TTGGACGATGGGAACTTCAAATTTCTTCTTCTTTGTGACATTTCCCTGATCTACGGTG CTACTGTGGTGGGAAACATTCTCATTATGGTCACAGTGACAGTAGTTCGACCCTTC ATTCTCCCTTGTACTTTCTCCTTGGAAATCTCTCTTTTTGGACATGTGTCTCTCCAC TGCCACAACACCCAAGATGATCCACAAGACCATCTCTGTGTGGGGCTGCGTGACCC AGAAGTTCTTCATGCACTTCTTTGGGAGTGCTGAGATGACTCTTCTGATAATCATGG CCTTTGACAGGTATGTAGCCATATGTAAACCCCTGCACTATAGGACAATCATGAGCC ACAAGCTGCTAAAGGGGTTTGCGATACTTTCATGGATAATTGGTTTTTTACACTCCA TAAGCCAGATAGTTTTAACAATGAACTTGCCTTTCTGTGGCCACAATGTCATAAACA ACATATTTGTGATCTTCCCCTTGTGATCAAGCTTGCTTGCATTGAAACATACACCC TGGAATTATTTGTCATTGCTGACAGCGGGCTGCTCTCTTTCACCGTGTTTCATCCTCTT GCTTGTTGTTTACATTGTCATCCTGGTCAGTGTACCCAAAAAAATCATCACACATGGGCT CTCCAAGGCGCTGTCCACATTGTCTGCCCACATCATTGTGGTCACTCTGTTCTTTGG ACCTTGTATTTTATCTATGTTTGGCCATTCAGTAGTTTGGCAAGCAATAAAACTCT TGCTGTATTTTATACAGTTATCACACCGTTACTGAATCCGAGTATTTATACCCTGAG AAATAAGAAAATGCAAGAGGCCATAAGAAGAAAATTACGGTTCCAATATGTTAGTTCTG CACAGAATTTCTAGAT	MNLKNGSLVTEFILLGFFGR WELQIFFVTFSLIYGATVV GNILIMVTVTCSSTLHSPLY FLLGNLSFLDMCLSTATTPK MIHKTISVWGCVTQKFFMH FFGSAEMTLLIIMAFDRYVA ICKPLHYRTIMSHKLLKGFA ILSWIIGFLHSISQIVLTMNLP FCGHNVINNIFCDLPLVIKL ACIETYTLELFVIADSGLLSF TCFILLVSYIVILVSVPKKS SHGLSKALSTLSAHIIVTLF FGPCIFIYVWPFSSLASNKTL AVFYTVITPLLNPSIYTLRN KKMQEAIRKLRFQYVSSAQ NF

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL359218_D	145/146	TCTGAAACCTGAGGCAATGGACCCACAGAACTATTCCTTGGTGTCAGAATTTGTGTT GCATGGACTCGCACTTCAGGACATCTTCAAAATTTTTCTTTATATTTTCTTTGGG GTCTATGTGGCCATTATGCTGGGTAACCTTCTCATTTGGTCACTGTAATTTCTGAT CCCTGCCTGCACTCCTCCCCTATGTACTTCCTGCTGGGGAACCTAGCTTCCTGGAC ATGTGGCTGGCCTCATTTGCCACTCCCAAGATGATCAGGGATTCCTTAGTGATCAA AAACTCATCTCCTTTGGAGGATGTATGGCTCAAATCTTCTTCTTGCACTTTACTGGT GGGGCTGAGATGGTGCTCCTGGTTTCCATGGCCTATGACAGATATGTGGCCATATG CAAACCCTTGCATTACATGACTTTGATGAGTTGGCAGACTTGCATCAGGCTGGTGCT GGCTTCATGGGTCGTTGGATTTGTGCACTCCATCAGTCAAGTGGCTTCACTGTAAA TTTGCCTTACTGTGGCCCAATGAGGTAGACAGCTTCTTCTGTGACCTCCCTCTGGT GATCAAACTTGCCTGCATGGACACCTATGTCTTGGGTATAATTATGATCTCAGACAG TGGGTTGCTTTCCTTGAGCTGTTTCTGCTCCTCCTGATCTCCTACACCGTGATCCTC CTCGCTATCAGACAGCGTGCTGCGCCGGTAGCACATCCAAAGCACTCTCCACTTGCTCT GCACATATCATGTAGTGACGGCTGTTCTTTGGCCCTTGCATTTTGTTTATGTGCGG CCTTTCAGTAGGTTCTCTGTGGACAAGCTGCTGTCTGTGTTTTATACCATTTTTACTC CACTCCTGAACCCCATTATCTACACACATTGAGAAAATGAGGAGGAGAGTGAAAGCAGCTATG AAGAAACTGCAAAACCGACGGGTGACTTTTCAATGAAATCCAGCCTTCCATA	MDPQNYSLVSEFVLHGLCT SRHLQNFFIFFFGVYVAIM LGNLLILVTVISDPCLHSSPM YFLLGNLAFLDMWLASFAT PKMIRDFLSDQKLISFGGCM AQIFFLHFTGGAEMVLLVS MAYDRYVAICKPLHYMTL MSWQTCIRLVLASWVVGFV HSISQVAFTVNLPYCGPNEV DSFFCDLPLVIKLACMDTYV LGIIMISDSGLLSLSCFLLLLI SYTVILLAIRQRAAGSTSKA LSTCSAHIMVVTLFFGPCIFV YVRPFSRFSVDKLLSVFYTIF TPLLNPIIYTLRNEEMKAAM KKLQNRRVTFQ

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAL359218_A	147/148	TAAAATGGATCTTAAAAAATGGATCTCTAGTGACCGAGTTTATTTTACTAGGATTTTT GGACGATGGGAACTTCAAATTTTCTTCTTTGTGACATTTTCCCTGATCTACGGTGCT ACTGTGATGGGAAACATTCTCATTATGGTCACAGTGACATGTAGGTCAACCCTTCAT TCTCCCTTGTACTTTCTCCTTGGAAATCTCTCTTTTTTGGACATGTGTCTCTCCACTG CCACAACACCCAAGATGATCATAGATTTGCTCACTGACCACACAAGACCATCTCTGTGT GGGGCTGCGTGACCCAGATGTTCTTCATGCACTTCTTTGGGGGTGCTGAGATGACTC TTCTGATAATCATGGCCTTTGACAGGTATGTAGCCATATGTAAACCCCTGCACTATA GGACAATCATGAGCCACAAGCTGCTAAAGGGGTTTGCGATACTTTCATGGATAATT GGTTTTTTACACTCCATAAGCCAGATAGTTTTAACAATGAACTTGCCTTTCTGTGGC CACAATGTCATAAACAACATATTTGTGATCTTCCCCTTGTGATCAAGCTTGCTTGC ATTGAAAACATACACCCTGGAATTATTTGTCATTGTCATCCTGGTCAGTGTACCAAAAA ACCTGTTTCATCCTCTTGCTTGTTCTTACATTGTCATTGTCTGCCACCATCATTGTGG AATCATCACATGGGCTCTCCAAGGCGCTGTCCACATTGTCTGCCCACATCAGTGTGG TCACTCTGTTCTTTGGACCTTGTATTTTATCTATGTTTGGCCATTCAGTAGTTTGGC AAGCAATAAAACTCTTGCCGTATTTTATACAGTTATCACACCCTTACTGAATCCGAG TATTTATACCCTGAGAAATAAGAAAATGCAAGAGAGGCCATAAGAAAATTACGGTTCC AATATGTTAGTTCTGCACAGAATTTCTAGAT	MDLKNGSLVTEFILLGFFGR WELQIFFVTFSLIYGATVM GNILIMVTVTCRSTLHSPLY FLLGNLSFLDMCLSTATTPK MIIDLLTDHKTISVWGCVTQ MFFMHFFGGAEMTLLIMA FDRYVAICKPLHYRTIMSHK LLKGFAILSWIIGFLHSISQIV LTMNLPFCGHNVINNIFCDL PLVIKLACIETYTLELFVIAD SGLLSFTCFILLLVSYIVILVS VPKKSSHGLSKALSTLSAHII VVTLFFGPCIFIYVWPFSSLA SNKTLAVFYTVITPLLNPSIY TLRNKKMQEAIRKLRFQYV SSAQNF

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC006313_A	149/150	GATGAACTCAGAGAGAACCTCACCCGGCCGGCCGGTTGCCCCTGCTGAATTCGTCCTCCT GGGCATCACAAATCGCTGGGACCTGCGTGTGGCCCTGTTCCTGACCTGCCTGCCTGT CTACCTGGTGAGCCTGCTGGGAAACATGGCATGGCCGCTGCTGATCCGACATGGATG CCCGGCTCCACACACCTATGTACTTCTTCCTGGCCAACCTCTCCCTGCTGGATGCCT GCTATTCCTCCGCCATCGGCCCCAAGATGCTAGTGGACCTGGACCTGGCCCCGAGCCA CCATCCCCTTACACAGCCTGTGCCCTCCAGATGTTTGTCTTTGCAGGTCTGGCTGATA CTGAGTGTTGCTTGCTGGCAGCCATGGCCTATGACCGCTACGTGGCCATCAGAAAC CCACTTCTCTATACAACAGCTATGTCGCAGCGTCTATGCCTGGCCTTGCTGGGAGCA TCAGGCCTGGGTGGGGCAGTGAGTGCCTTTGTTCACACAACCCTCACCTTCCGCCTG AGCTTCTGCCGCTCCCGGAAGATCAATAGCTTCTTCTGCGATATCCCTCCACTGCTG GCCATCTCGTGCAGTGACACCAGTCTCAATGAACTCCTTCTTCTTCGCCATCTGTGGC TTCATCCAGACAGCCACGGTGTTAGCTATCACGGTGTCTTATGGCTTCATCGCTGGG GCTGTGATCCACATGCGCTCGGTCGAGGCAGTCGGCGAGCAGCCTCACCGGTGG TTCCCACCTCACAGCCGTGGCCATGGCCATGATGTACGGGACACTCATTTCATGTACCTGCG CCCCAGCTCCAGTCCGTCTCTCAACCCACTCACTCATCTACAGCCTCCGCAATAAGGAGGTCAAGGA GGTCATCCCGTCTCTCAACCCACTCACTGCCACTGTCCAGGCAGGGTCCCAGTGAT GGCCCTCAGGCAGGACCTGGACCGATTCCACTGGTGCTGACTATGAGGGGATGAGGAAG TGGTCCAGGGAGGCTGGGTAGGTCTGACTATGAGGGGGATGAGGAAG	MNSENLTRAAVAPAEFVLL GITNRWDLRVALFLTCLPV YLVSLLGNMGMALLIRMDA RLHTPMYFFLANLSLLDAC YSSAIGPKMLVDLLPRATI PYTACALQMFVFAGLADTE CCLLAAMAYDRYVAIRNPL LYTTAMSQRLCLALLGASG LGGAVSAFVHTTLTFRLSFC RSRKINSFFCDIPPLLAISCSD TSLNELLLFAICGFIQTATVL AITVSYGFIAGAVIHMRSVE GSRRAASTGGSHLTAVAM MYGTLIFMYLRPSSSYALDT DKMASVFYTLVIPSLNPLIY SLRNKEVKEALRQTWSRFH CPGQGSQ

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
CG55970-01	151/152	TGGGGGGCTTTGGGACTAACATCTCAAGTACTACCAGCTTCACTCTAACAGGCTTCC CTGAGATGAAGGGTCTGGAGCACTGGCTGCTGCCCTTCTGCTGCTTTATGCTA TTTCCTTCCTGGGCAACATCCTCATCCTCTTTATCATAAAGGAAGAGCAGCTTGC ACCAGCCAATGTACTACTTCCTGTCTCTTTTTCTGTTAATGACCTGGGTGTGCCTT TTCTACAITGCCCACTGTACTGGCTGCTGTCTGTTTTCATGCCCCAGAGACAACTTT TGATGCCTGCCTGGCCCAGATGTTCTTCATCCACTTTTCCTCCTGGACAGAGTTTGG CATCCTACTGGCCATGAGTTTTGACCACTATGTGGCCATCTGTAACCCGCTGCGCTA TGCCACAGTGCTCACTGATGTCCGTGTGGCCCACAATGGCATATCCATTGTCATCCG CAGCTTCTGCATGGTATTCCCACTTCCCTCCTCCTACTGTCTGCATGCAGACCTGATTGGCTGCC GGCCAGTGTGGTACTGGCCCCATTCCTACTGTCTGCATGCAGACCTGATTGGCTGCC CTGGGGAGACACTACCATCAACAGCATGTATGGCCTGTTCATTGTCATCTCTGCCTT TGGTGTAGATTCACTGCTCATCCTCCTCTATGTGCTCATTCTGCGTTCTGTGCTG GCCATTGCCTCCAGGGGTGAGAGGCTTAAGACACTCAACACATGTGTCACATAT CTATGCAGTGCTGAICTTCTATGTGCTAIGGTTGGTGTCCATGGTTCATCGATT TGGGAGGCATGCTCCTGAATATGTGCACAAGTTCATGTCTCTTTGTACCTCCAATGC TCTACCCAAITTAITCTATTCCATCAAGACTAAGGAGATTCGCAGGAGACTACACA	GGFGTNISSTTSFTLTGFPE MKGLEHWLAALLLLYAIS FLGNILILFIIKEEQSLHQPM YYFLSLFSVNDLGVSFSTLP TVLAAVCFHAPETTFDACL AQMFFIHFSSWTEFGILLAM SFDHYVAICNPLRYATVLTD VRVAHNGISIVIRSFCMVFP LPFLLKRLPFCKASVVLAHS YCLHADLIRLPWGDTTINS MYGLFIVISAFGVDSLLILLS YVLILRSVLAIASRGERLKT LNTCVSHIYAVLIFYVPMVG VSMVHRFGRHAPEYVHKF MSLCTSNALPNYLFHQD

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
CGS59396-01	153/154	AATTATCCAAATACCAAACTGGATTTCGAGCAAGTGAACAACATAACGGAATTCAT CTTGCTTGGCCTGACACAGAACGCAGAGGCACAGAAACTCTTGTTTGCTGTGTTTAC ACTCATCTACTTTCTCACCATGGTAGACAACCTAATCATTGTGGTGACAATCACCAC CAGCCCAGCCCTGGACTCCCCCGTGTATTTTTTCGTGCTTTCTTTCTTCATAGAT GGCTGCTCCTCTTCTACCATGGCCCCCAAAATGATATTTGACTTACTCACTGAAAAG AAAACTATTTCCTTCAGTGGGTGCATGACCCAGCTCTTTGTAGAACATTTCTTTGGG GGAGTTGAGATCATTCTGCTCGTGGTGATGGCCTATGACTGCTATGTGGCCATCTGC AAGCCCCTGTACTACCTGATCACAATGAACAGGCAGGTATGTGGCCTCCTGGTGGC CATGGCATGGTCGGGGGGATTTCTTCACGCTCTGATTCAAATGCTTTTAATAGTCTG GCTGCCCTTCTGTGGCCCCAATGTCATTGACCATTTCATCTGTGACCTTTTCCCTCTG CTAAAACTCTCCTGCACTGACACTCACGTCTTTTGGACTCTTTGTTGCCGCCAACAGT GGGCTGATGTGTATGCTCATTTTTTCTATTCTTTATTACCTCTACGTCTAATCCTCT GCTCACAGCGGAAGGCTCTCTCTCTACCTGCGCCTTCCATATCACTGTAGTCGTCCTAT TCTTTGTTCCCTGTATATTGGTGTACCTTCGACCATCCCCTATTGATAA AGCTGTGTCTGTGTTTTATACTGTGGTAACACCCATGTTAAACCCTTTAAATCTACAC CCTCAGAAACACAGAGGTGAAAAATGCCATGAAGCAGCTCTGGAGCCAAATAATCT GGGGTAACAATTTGTGTGATTAGAGAAGATAAACACAGAACCTACTCATATTTTAA CAACAG	NYPNTKLDFEQVNNITEFIL LGLTQNAEAQKLLFAVFTLI YFLTMVDNLIIVTITTSPAL DSPVYFFLSFFSFIDGCSSST MAPKMIFDLLTEKKTISFSG CMTQLFVEHFFGGVEIILLV VMAYDCYVAICKPLYYLIT MNRQVCGLLVAMAWVGGF LHALIQMLLIVWLPFCGPNV IDHFICDLFPLLKLSCTDTHV FGLFVAANSGLMCMLIFSILI TSYVLILCSQRKALSTCAFHI TVVVLFFVPCILVYLRPMIT LPIDKAVSVFYTVVTPMLNP LIYTLRNTEVKNAMKQLWS QIIWGNNLCD

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC076959_A	155/156	AACATGGAAAGCAATCAGACCTGGATCACAGAAGTCATCCTGTTGGGATTCCAGGT GGACCCAGCTCTGGAGTTGTTCCTCTTTGGGTTTTTCTTGCTATTCTACAGCTTAACC CTGATGGGAAATGGGATTATCCTGGGGCTCATCTACTTGGACTCTAGACTGCACAC ACCCATGTATGTCTTCCGTCACACCTGGCCATTGTGGACATGTCCTATGCCTCGAG TACTGTCCCTAAGATGCTAGCAAATCTTGTGATGCACAAAAAGTCATCTCCTTTGC TCCTTGCATACTTCAGACTTTTTGTATTGGCGTTTGCTATTACAGAGTGTCTGATT TTGGTGATGATGTGCTATGATCGGTATGTGGCAATCTGTCACCCCTTGCAATACACC CTCATTATGAACTGGAGAGTGTGCACTGTCCTGCCTCAACTTGCTGGATATTTAGC TTTCTCTTGGCTCTGGTCCATATTACTCTTATTCTGAGGCTGTTTTTGTGGCCCAC AAAAGATCAACCACTTTTTCTGTCAAATCATGTCCGTATTCCGTATTCAAATTGGCCTGTGCTG ACACTAGGCTCAACCAGGTGGTCCTATTTGCGGTTCTGCGTCATCCTGGTGGGC CGCTCTGCCTGGTCGTGGTCTCCTACTTGCACATCCTGGTGGCCATCTTGAGGATCC AGTCTGGGGAGGGGCCGCAGAAAGGCCTTCTCTACCTGCTCCTCCCACCTCTGCGTGG TGGGGCTTTTCTTTGGCAGCGCCATTGTCATGTACATGGCCCCCAAGTCAAGCCATT CTCAAGAACGGAGGAAGATCCTTTCCCTGTTTTACAGCCTTTCAACCGATCCTGA ACCCCCTCATCTACAGCCTTAGGAATGCAGAGGTGAAAGGGGCTCTAAAGAGAGTC CTTTGGAAACAGAGATCAATGTGAAGAATCATTTGAGATATCCTGA	MESNQTWITEVILLGFQVDP ALELFLFGFFLLFYSLTLMG NGIILGLIYLDSRLHTPMYV FLSHLAIVDMSYASSTVPK MLANLVMHKKVISFAPCIL QTFLYLAFAITECLILVMMC YDRYVAICHPLQYTLIMNW RVCTVLASTCWIFSFLLALV HITLILRLPFCGPQKINHFFC QIMSVFKLACADTRLNQVV LFAGSAFILVGPLCLVLVSY LHILVAILRIQSGEGRRKAFS TCSSHLCVVGLFFGSAIVMY MAPKSSHSQERRKILSLFYS LFNPILNPLIYSLRNAEVKG ALKRVLWKQRSM

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC076959_C	157/158	CATGGAAGGCAACAAGACACATGGATCACAGAGACATCACCTTGCCGCGATTCCAGGTTG GTCCAGCACTGGAGATTCTCCTCGTGGACTTTTCTCTGCCTTCTATACACTCACCCT GCTGGGGAATGGGGTCATCTTTGGGATTATCTGCCTGGACTGTAAGCTTCACACACC CATGTACTTCTTCCTCACACCTGGCCATTGTTGACATATCCTATGCTTCCAACTAT GTCCCCCAAGATGCTGACGAATCTTATGAACCAGGAAAGCACCATCTCCTTTTTCCA TGCATAATGCAGACATTCTTGTATTTGGCTTTTGCTCACGTAGAGTGTCTGATTTTG GTGGTGATGTCCTATGCGGACATCTGCCACCCTTACGTTACAATATC CTCATGAGCTGGAGAGTGTGCACTGTCCTGGCTGTGTGGCTTCAGCTTC CTCCTGGCTCTGGTCCCTTAGTTCTCATCCTGTGTCTCCTC GAAATCAACCACTTCTGTGAAATCCTGTCTGTCCTCAAGTTGGCCTGTGCTGACACC TGGCTCAACCAGGTGGTCATCTTTGCAGCCTGCGTGTTCATCCTGGTGGGGCCACTC TGCCTGGTGCTGGTCTCCTACTTGCGGCATCCTGGCCGCCATCTTGAGGATCCAGTCT GGGGAGGGGCGCAGAAAGGCCTTCTCCACCTGCTCCTCCCACCTTTGCGTGGTGGG ACTCTTCTTTGGCAGCGCCATTGTACATGTCACGTACATGGCCCCCAAGTCCCGCCATCCTGA GGAGCAGCAGAAAGTTCTTCCCGTGTTTTACAGCCTTTCAATCCAATGCTGAACCC CCTGATATATAGCCTAAGGAATGCAGAGGTCAAGGGCGCCCCTGAGGAGGAGGCACTGA GGAAGGAGAGGCTGACGTGAGACATCTCAAAG	MEGNKTWITDITLPRFQVGP ALEILLCGLFSAFYTLTLLG NGVIFGIICLDCKLHTPMYF FLSHLAIVDISYASNYVPKM LTNLMNQESTISFFPCIMQT FLYLAFAHVECLILVVMSY DRYADICHPLRYNILMSWR VCTVLAVASWVFSFLLALV PLVLILRLPFCGPHEINHFCE ILSVLKLACADTWLNQVVIF AACVFILVGPLCLVLVSYLR ILAAILRIQSGEGRRKAFSTC SSHLCVVGLFFGSAIVTYMA PKSRHPEEQQKVLSLFYSLF NPMLNPLIYSLRNAEVKGA LRRALRKERLT

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Table 1

Acc. No.	SEQ ID NO (Nucl)/SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC076959_D	159/160	GAATGGGGAGTCAACCAATCATGGGTCACAGAATTCATCCTGGTGGGGATTCCAGCTC AGTGCCGGAGATGGAAGTGCTCCTCTTTTAGATCTTCTCCCTGTTATACATCTTCAGC CTGCTGGCAAATGGCATGATCGTGGGACTCATCTGTCTGGACCACATTCTGCCTACC CCCATGTACTTCTTCCTCTCACACCTGGCCATCATTGACATGTCCTATGCTTCCAACA ATGTTCCCAAGATGTGGCAAATCTGATGAACAAGAAAAAGAACCATCTCCTTTCTTC CATGCATAATGCAGACCTATTTGTATTTGCTGCTACAGAGTGTCTGATTTT GGTGGTGATGTCCTATGATAGGTATGTGCCCATTTGCCACCCTCTCCAGTACACTGT CATCATGAGCTGGAGAGTGTGCACGATCCTGGCTCTCACATCCTGGTCATGTGGGTT TGCCCCTGTCCCGGTACATGCAATTCTTCTTCTGTGCTCCTGAAATTCGTCTGTCTCCTGA GGATGTGAACCACCTCTTCTGTGAAATTCGTCTGTCTCCTCAAGCTGGCCTGTTCTGA CACCTGGGTTAACCAAGTGGTCATATTGCTACCTGTGTTGTTTGCTTAGTTGGACC TCTTTGTTTGATGCTTGTCTCCTACACTGCACATCCTCTGGCCATCCTCCCACCTGTGTGTGG GACAAAGGAAGGCCGCATAAAGGCCTTCTCGACCTGCTCCTCCCACCTGTGTGTGG TTGGACTCTTCTTTTGGCATAGCCATGGTGTTTACATAGTCCCAGACTCTAATCAAC GAGAGGAGCAGGAGGAGAAAATGCTGTCCCTGTTCACAGTGTCTTGAACCAATTCTG AACCCCTGATCTACAGTCTGAGGAATGCTCAGGTGAAGGGCGCCCCTCCACAGAGC ACTGCAGAGGACGACGCTGTCTATGTAAGGA	MILGLICLDHILPTPMYFFLS HLAIIDMSYASNNVPKMLA NLMNKKRTISFLPCIMQTYL YFSFAATECLILVVMSYDRY VAICHPLQYTVIMSWRVCTI LALTSWSCGFALSLVHAILL LRLPFCGPRDVNHLFCEILS VLKLACSDTWVNQVVIFAT CVFVLVGPLCLMLVSYMHI LWAILKIQTKEGRIKAFSTC SSHLCVVGLFFGIAMVVYIV PDSNQREEQEKMLSLFHSV LNPILNPLIYSLRNAQVKGA LHRALQRTLSM

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP000818_A_3	161/162	GACTGGCTTCCATGGAGGTGAAGAACTGCTGCATGGTGACAGAGTTCATCCTTTTG GGAATCCCACACACAGAGGGGCTGGAGATGACACTTTTGTCTTATTCTTGCCCTTC TATGCCTGCACTCTACTGGGAAATGTGTCTATCCTTGTTGCTGTTATGTCTTCTGCTC GCCTTCACACACCTATGTATTTCTTCCTGGGAAACTTGTCTGTGTTTGACATGGGT TCTCCTCAGTGACTTGTCCCAAAATGCTGCTCTCACCTTATGGGGCTGAGCCGACTCA TCTCCTACAAAGACTGTGTCTGCCAGCTTTCTTCTTCCATTCCTGGGAGCATTGA GTGCTTCTTGTTTACGGTGATGGCCTATGACCGGCTTCACTGCCATCTGTTATCCTCTG CGATACACAGTCATCATGAACCCAAGGATCTGTGTGGCCCTGGCTGTGGGCACATG GCTGTTAGGGTGCATTCATTGAAGTGGATCACTTCTTGACCTCCCTCACCTTGCCCTT CTGTGGTCCCAATGAAGTGGATCACATCCTTAGCCCAGAGGGTGAGCTTCACCAACGTTGGCCTCAT GGCCTGTGCTGACACATCCTTAGCCCAGAGGGTGAGCTTCACCAACGTTGGCCTCAT ATCTCTTGTCTGCTTTCTGCTAATTCTTTTATCCTACACTAGAATCACAATATCTATC TTAAGCATTCGTACAACTGAGGGCCGTCGCCGTCTCCCACCTGCCAGTGCTCAC CTCATTGCCATCCTCTGTGCCTATGGCCCATCATCACTGTCTACCTGCAGCCCACA CCCAACCCCATGCTGGGAACCGTGGTACAAATTCTCATGAATCTGGTAGGACCAAT GCTGAACCCTTTGATCTATACCTTGAGGAATAAGGAAGTAAAAACAGCCCTGAAAA CAATATTGCACAGGACAGGCCATGTTCCTGAGAGTTAGTAAGAGCAGATAAATGG	MEVKNCCMVTEFILLGIPHT EGLEMTLFVLFLPFYACTLL GNVSILVAVMSSARLHTPM YFFLGNLSVFDMGFSSVTCP KMLLYLMGLSRLISYKDCV CQLFFHFLGSIECFLFTVM AYDRFTAICYPLRYTVIMNP RICVALAVGTWLLGCIHSSI LTSLTFTLPYCGPNEVDHFF CDIPALLPLACADTSLAQRV SFTNVGLISLVCFLILLSYT RITISILSIRTTEGRRRAFSTC SAHLIAILCAYGPIITVYLQP TPNPMLGTVVQILMNLVGP MLNPLIYTLRNKEVKTALK TILHRTGHVPES

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GM524k20_A	163/164	GAATTATATATACCTGAATGAAAACGAGAGGCTGGAATCATACAGGTGCAAAGGAA TTCCTCCTGGTAGGGTTAACTGAAAAATCCTAATTGCAGATCCCACTCTTTTGCTT GTCACTCTGATTTATTTCATCACTTTGTTGGATAATTTGGGTATAATTATTTTAATCT GGTTAAAATGCCAACTTCATACTCCAATGTACTTCTTCCTTGGCAACCTCTCCTTTTG TGATATCTGCTACTCACTGTCTTTGCTCCTAAGATGCTAGTCAATTCCTATCAAA ACATAAGTCCAGTACATTTTCTGGCTGTGTTCTACAGAGTTTCCCTTTGCAGTATA TGTAACCACAAAGGACATTCTCCTGTCCATGATGGCTTATGACCATTACGTGGCCAT AGCTAATCCCTTGTTGTATACAGTCATTATGGCCCAAAAAGTTTGTATTCAGATGGT CCTTGCTTCTTACTTAGGTGGGCTCATTAATTCCCTGACACACAATAGGTTTGCT CAAATTAGACTTCTGTGGTCCTAATATTGTGAATCATTATTTCTGTGATGTTCCTCCT CTTCTGAGGCTTTCTTGCTCGTGATGCTCATATCAATCAATGAAATGCTGCCCTTGGTCTTCT CTGGGCTCATTGCAAATGTTCACTTCATTGTCATTATGGTGTCTTATATCTGCATCAT CATTGCCATCCAGAGAATCCATGCAGCTGAGGGAAGGTACAAAGCCTTCTCCACTT GTGTCTCCCACCTAACCACGGTGACCTTATTCTATGGGTCTGTTTCTTTTAGTTATAT CCAGCCAAGTTCTCAGTATTCCTTGGAACAGGAGAAGGTCTTGGCTGTGTTTTTATAC ACTGGTGATCCCCATGCTAAACCCACTTATTTATAGCCTGAGAAATAAGGATGTAA AAGATGCAGCCAAAAGGTTGATATGGTGGGGGAAAAACCCCACTTGACTCAGTCC TGCATATAGCTTTGCTAACCTAACATTTACCTGCAAATATATGGCCTATCTTTAAAA	MKTRGWNHTGAKEFLLVG LTENPNLQIPLFLLVTLIYFIT LLDNLGIILIWLNAQLHTP MYFFLGNLSFCDICYSTVFA PKMLVNFLSKHKSSTFSGC VLQSFPFAVYVTTKDILLSM MAYDHYVAIANPLLLYTVIM AQKVCIQMVLASYLGGLIN SLTHTIGLLKLDFCGPNIVN HYFCDVPPLLRLSCSDAHIN EMLPLVFSGLIAMFTFIVIM VSYICIIIAIQRIHAAEGRYK AFSTCVSHLTTVTLFYGSVS FSYIQPSSQYSLEQEKVLAV FYTLVIPMLNPLIYSLRNKD VKDAAKRLIWGEKPHLT QSCI

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GM563n7_A	165/166	GCCGTGTTCTTCGCCCTGTTCCTGGGCATGTACCTGACCACGGTGCTGGGGAACCTG CTCATCATGCTGCTCATCCAGCTAGACTCTCACCTTCACCACCCCATGTACTTCTTCC TTAGCCACTGGCCCTCACTGACATCTCCTTTCATCTGTCCCTAAGATGCT GATGAACATGCAGACTCAGCACCTAGCCGTCTTTTACAAGGGATGCATTCACAGA CATATTTTTCATATTTTTGCTGACTTAGACAGTTTCCTTATCACTTCAATGGCATA TGACAGGTATGTGGCCATCTGTCATCCTCTACATTATGCCACCATCATGACTCAGAG CCAGTGTGTCATGCTGGTGGCTGGGTCATCGTTGTGCGTGTCTCTTTT GCATACCCTCCTGGCCCAGCTTTCCTTCTGTGCTGACCACATCATCCCTCACTAC TTCTGTGACCTTGGTGCCCTGCTCAAGTTGTCCTGCTCAGACACCTCCCTCAATCAG TTAGCAATCTTTACAGCAGCATTGACAGCCATTATGCTTCCATTCCTGCATCCTG GTTTCTTATGGTCACATTGGGGTCACCATCTCCTCTACCAAGGGCATA TGCAAGCCTTGTCCACTTGTGGATCCCCATCCAGTTGGTGACTATCTATTATCGG ACAATTATTGGTCTCTATTTTCTTCCCCCATCCAGCAACACCAATGACAAGAACATA ATTGCTTCAGTGATATACACAGACAGTAAGGGAGCCCTAAGAAAACTCTTGAGTAGGTCAGGCGC AGTGGCTCATGCCTGTAATCTCAGCACTTGGGAGGCTGAGGCAGAC	MYLTTVLGNLLIMLLIQLDS HLHTPMYFFLSHLALTDISF SSVTVPKMLMNMQTQHLA VFYKGCISQTYFFIFFADLDS FLITSMAYDRYVAICHPLHY ATIMTQSQCVMLVAGSWVI ACACALLHTLLLAQLSFCA DHIIPHYFCDLGALLKLSCS DTSLNQLAIFTAALTAIMLP FLCILVSYGHIGVTILQIPST KGICKALSTCGSHLSVVTIY YRTIIGLYFLPPSSNTNDKNI IASVIYTAVTPMLNPFIYSLR NKDIKGALRKLLSRSGAVA HACNLSTLGG

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GM656o22_B	167/168	CCCTGTGCTCTTCCCACAGGTGGCCTTTTGCCCACCCCCAGCATACAATGATGGAA ATAGCCAATGTGAGTTCTCCAGAAGTCTTTGTCCTGGGCTTCCACACGACCC TCACTAGAAACTGTCCTCTTCATAGTTGTCTTGAGTTTTTACATGTATCGATCTTG GGCAATGGCATCATCATTCTGGTCTCCATACAGATGTGCACCTCCACACCTATG TACTTCTTTCTTGCCAACCTCCCCTTCCTGGACATGAGCTTCACCAGCATTGTCC CACAGCTCCTGGCTAACCTCTGGGGACCACAGAAAACCATAAGCTATGGAGGGTGT GTGGTCCAGTTCTATATCTCCCATTGGCTGGGGCAACCGAGTGTGTCCTGCTGGCC ACCATGTCCTATGACCGGCTACGCTGCCATCTGCAGGCCACTCCATTACACTGTCATT ATGCATCCACAGCTTTGCCTTGGGCTAGCTTGGCCTCCTGGCTGGGGGTCTGACC ACCAGCCATGGTGGGCTCCACGCTCACCATGTCTCCTACGCTGTGTGGGAACAATTG CATCGACCACTTCTTTTGCGAGATGCCCCTCATTATGCAACTGGCTTGTGTGGATAC CAGCCTCAATGAGGATGGAGATGTACCTGGCCAGCTTTGTCTTTGTTGTCCTGCCTCT GGGGCTCATCCTGGTCTCTTACGGCCACATTGCCCGGGCCGTGTTGAAGATCAGGTC AGCAGAAGGGCGGAGAAAGGCATTCAACACCTGTTCTTCCCACGTGGCTGTGGTGT CTCTGTTTTACGGGAGCATCATCTTCATGTATCTCCAGCCAGCCAAGAGACACCTCCC ATGAGCAGGGCAAGTTCATAGCTCTGTTCTACACCGTAGTCACTCCTGCGCTGAACC CACTTATTTACACCCTGAGGAACACGGAGGTGAAGAGCGCCTCCGGCACATGGTA TTAGAGAACTGCTGTGTGGCTCTGCAG	MMEIANVSSPEVFVLLGFST RPSLETVLFIVVLSFYMVSIL GNGIIILVSHTDVHLHTPMY FFLANLPFLDMSFTTSIVPQL LANLWGPQKTISYGGCVVQ FYISHWLGATECVLLATMS YDRYAAICRPLHYTVIMHP QLCLGLALASWLGGLTTSM VGSTLTMLLPLCGNNCIDHF FCEMPLIMQLACVDTSLNE MEMYLASFVFVLPLGLILV SYGHIARAVLKIRSAEGRRK AFNTCSSHVAVVSLFYGSIIF MYLQPAKSTSHEQGKFIALF YTVVTPALNPLIYTLRNTEV KSALRHMVLENCCGSA

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC009779_A	169/170	ACTCAAAATTTTTCAACAATGAAAAATAAAACCGTGTTAACTGAGTTTATCCTTCT GGGTCTAACAGATGTCCCTGAACTCCAGGTGGCAGTTTCACCTTTCTTTCCTTGC GTATTACTCAGCATCCTTGGAAATCTGACTATCCTCATCCTCACCTTGCTGGACTC CCACCTTCAGACTCCCATGTATTTCTTTCTCCGGAACTTCTCCTTCTTGGAAATTTCC TTCACAAACATCTTCATTCCAAGGGTCCTGATTAGCATCACAACAGGGAACAAGAG TATCAGCTTTGCTGGCTGCTTCACTCAGTATTTCTTTGCCATGTTCCTTGGGGCTACA GAGTTTTACCTTCTGGCTGCCATGTCCTATGTGACCGCTATGTGGCCATCTGCAAACCT CTGCATTACACCACCATCATGAGCAGCAGAATCTGCATCCAGCTGATTTCTGCTCT TGGCTGGGTGGGCTAAATGGCTATTATACCAACAATCACCCTGATGAGTCAGCAGGA CTTTTGTGCATCCAACAGACTGAATCATTACTTCTGTGACTATGAGCCTCTTCTGGA ACTCTCATGTTCAGACACAACAAGCCTCATAGAGAGAAGGTTGTCTTTCTTGTGGCATCTGT GACCCTGGTGGTCACTCTGGTGTGCTAGTGATTCTCTCCTATGCATTCATTATCAAGAC TATTCTGAAGCTCCCCCTCTGCCCAACAAAGGACAAAAGCCTTTCCACATGTTCTTC CCACATGATTGTCATCTCCCCTCTTACGGAAGCTGCATGTTTATGTACATTAATCC CTCTGCAAAGAAGAGGGGATACATTCAACAAGGGAGTAGCTCTACTCATTACTTCAG TTGCTCCTTTGTTGAACCCCTTTATTACACCCTAAGGAACCAACAGGTAAAACAAC CCTTCAAGGGATATGGTCAAAAAGCTTCTGAATCTTTAAAG	MKNKTVLTEFILLGLTDVPE LQVAVFTLFLAYLLSILGN LTILILTLLDSHLQTPMYFFL RNFSFLEISFTNIFIPRVLISIT TGNKSISFAGCFTQYFFAMF LGATEFYLLAAMSYDRYVA ICKPLHYTTIMSSRICIQLIFC SWLGGLMAIIPTITLMSQQD FCASNRLNHYFCDYEPLLEL SCSDTSLIEKVVFLVASVTL VVTLVLVILSYAFIIKTILKL PSAQQRTKAFSTCSSHMIVI SLSYGSCMFMYINPSAKEG DTFNKGVALLITSVAPLLNP FIYTLRNQQVKQPFKDMVK KLLNL

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC026975_B	171/172	GATACAAAATGTATGTCTGATTACTCTACACCACCCAAATTGCTGCCTCTTGATGAT GACCTCTTGGCTAACATACACAACATGACTGAATTCATTTTTCTGGTACTTTCTCCC AACCAGGAGGTGCAGAGGGTTTGCTTTGTGATATTTCTGTTCTTGTACACAGCAATT GTGCTGGGGAATTTCCTCATTGTGCTCACTGTCACTGTGCTCATGGTTCC CCCATGTACTTCTTCCTCAGCTACCTCCTCCTTCATGGAGATCTGCTACTCCTCCGCTA CAGCCCCCAAACTCATCTCAGATCTGGCTGCGGCTGAAAGGAAAGTCATATCTTGGTGG GGCTGCATGGCACAGCTTTTCTTCTTGCCACTTCTTTGGTGGCACTGAGATTTTCCTG CTCACTGTGATGGCCTATGACCACTATGTGGCCATCTGCAAGCCCCTCAGCTACACC ACCATCATGAACTGGCAGGTGTGTACTGTCCTTGTAGGAATAGCATGGGTGGGAGG CTTCATGCATTCCTTTGCACAAATCCTTCTCATCTTCCACCTGCTCCTTCTGTGGCCCC AATGTGATCAATCACTATTTCTGTGACCTAGTTCCCCTTCTCAAACTTGCCTGCTCTG ACACCTTCCTCATTGGTCTGCTGATTGTTGCCAATGGAGGCACCCTGTCTGTGATCA GTTTTGGGGTCCCTTAGCATCCTATATGGTCATCTTGCTCCATCTGAGAACCTGGA GCTCTGAAGGGTGGTGCAAAGCCCTCTCCACCTGTGGGTCCCATTTCGCTGTGGTTA TCTTGTTCTTTGGGCCCTGCGTCTTCAACTCTCAACTTCGCTTCTACCACTCTGCCCAT AGACAAGATGGTGGCTGTGTTCTACACACAGTGATAACCGGCATCCTGAACCCTGTCA TCTACTCTCTGAGAACTAAATGCTGAAAATGAGGAAGGCCATGAAGAGGCTGTGGATTAGG ACATTGAGAGACTAAATGAGAAATAGAGAGGCTGA	MSDYSTPPKLLPLDDDLLA NIHNMTEFIFLVLSPNQEVQ RVCFVIFLFLYTAIVLGNFLI VLTVMTSRSLGSPMYFFLSY LSFMEICYSSATAPKLISDLL AERKVISWWGCMAQLFFLH FFGGTEIFLLTVMAYDHYV AICKPLSYTTIMNWQVCTV LVGIAWVGGFMHSFAQILLI FHLLFCGPNVINHYFCDLVP LLKLACSDTFLIGLLIVANG GTLSVISFGVLLASYMVILL HLRTWSSEGWCKALSTCGS HFAVVILFFGPCVFNSLRPST TLPIDKMVAVFYTVITAILN PVIYSLRNAEMRKAMKRL WIRTLRLNEK

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Table 1

SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
Acc. No.		
GM824k2_A 173/174	AAACTTGGACGATCGACATGGAAATTGTCTCCACAGGAAACGAAACTATTACTGAA TTTGTCCTCCTTGGCTTCTATGACATCCCTGAACTGCATTTCTTGTTTTTTATTGTAT TCACTGCTGTCTATGTCTTCATCATCATAGGGAATATGCTGATTATTGTAGCAGTGG TTAGCTCCCAGAGGCTCCACAAACCCATGTATATTTTCTTGGCGAATCGTGTCCTTCC TGGATATTCTTCTACACCTCCGCAGTGATGCCAAAAATGCTGGAGGGCTTCCTGCAA GAAGCAACTATCTCTGTGGCTGGTTGCTGCTCCAGTTCTTTATCTTCGGCTCTCTA GCCACAGCTGAATGCTTACTGCTGGCTGTCATGGCATATGACCGGCTACCTGGCAATT TGCTACCCACTCCACTACCCACTCCTGATGGGGCCCAGACGGTACATGGGGCTGGT GGTCACAACCTGGCTCTCTGGATTTGTGGTAGATGGACTGGTTGTGGCCCTGGTGGC CCAGCTGAGGTTCTGTGGCCCCAACCACATTGACCAGTTTACTGTGACTTTATGCT TTTCGTGGGCCTGGCTGCTCGGATCCCAGAGTGGCTCAGGTGGCTCAGGTGGCTCAGGT GTCTGTGTTCTGCCTCACTATTCCTTTTGGACTGATTCTATGCCAGAATT GTGGTGGCAGTGCTGAGAGTTCCTGCTGGGCAAGCAGGAGAAGGGCTTTCTCAC ATGCTCCTCCCACCTAGCTGTAGTGACCACATTCTATGGAACGCTCATGATCTTTTA TGTTGCACCCTGTCACCCCTCTTCAATCCTGTGATCTATACCATGAGGAACAAGGAGGTG CATCAGGCACTTCGGAAGATTCTCTGTATCAAACAAACTGAAACACTGATTGAAG GAGA	MEIVSTGNETITEFVLLGFY DIPELHFLFFIVFTAVYVFIII GNMLIIVAVVSSQRLHKPM YIFLANLSFLDILYTSAVMP KMLEGFLQEATISVAGCLLQ FFIFGSLATAECLLLAVMAY DRYLAICYPLHYPLLMGPR RYMGLVVTTWLSGFVVDG LVVALVAQLRFCGPNHIDQ FYCDFMLFVGLACSDPRVA QVTTLILSVFCLTIPFGLILTS YARIVVAVLRVPAGASRRR AFSTCSSHLAVVTFYGTL MIFYVAPSAVHSQLLSKVFS LLYTVVTPLFNPVIYTMRN KEVHQALRKILCIKQTETLD

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001804_C_1	175/176	GAACATAAATGCCTTAAATGACAATGGCTGCTGAGAATTCCTCCTTCGTGACACAG TTTATCCTGCCAGGCTTAACTGACCAACCGGGAGTCCAGATCCCCCTCTTCTTCCTG TTTCTAGGCTTCTACGTGGTCACTGTGGTGGGAACCTGGCTTGATAACCCTGATA AGGCTCAACTCTCACTTGCACACCCCTATGTACTTCTTCCTCTATAAACTTGTCCTTCA TAGATTTCTGCTATTCCAGTGTTATCACTCCCAAAATGCTGATGAGCTTTGTCTTAA AGAAGAACAGCATCTCCTACGCAGGGTGTATGACTCAGCTCTTCTTCTTTTTCT TTGTTGTTCTCTGAGTCCTTCATCCTGTCAGCAATGGCGTATGACCGGCTATGTGGCCA TCTGTAACCCACTGTTGTACATGGTCACATGTCTCCCCAGGTGTGTTTTCTCCTTTT GTTGGGTGTCTATGGGATGGGGTTTGCTGGGGCCATGGCCCACACAGCGTGCATGA TGGGTGTGACCTTCTGTGCCAATAACCTTGTCAACCACTACATGTGTGACATCCTTC CCCTTCTTGAGTGTGCTTGCACCAGCACCTATGTGAATGAGCTTGTAGTGTTTGTTG TTGTGGGCATTGATATTGGTGTGCCCACAGTCACCATCTTCATTTCCTATGCTCTCA TTCTCTCCAGCATCTTCCACATTGATTCCACGAGGGCAGGTCCAAAGCCTTCAGCA CCTGCAGCTCCCACATAATTGCAGTTTCTGTTCTTTGGGTCAGGAGCATTCATGT ACCTCAAACCCTTTCTCTTTTTAGCTATGAACCAGGCAAGGTGTTCTTCCCTATTCT ATACCACTGTGGTGCCCATGCTCAACCCATTAATTTATAGCCTGAGGAATAAGGAC GTCAAAGTTGCTCTAAAGAAAATCTTGAACAAAAATGCATTCTCCTGAGAAAAGGG CAATGCTCAGGAAAGAAACACT	MTMAAENSSFVTQFILAGL TDQPGVQIPLFFLFLGFYVV TVVGNLGLITLRLNSHLHT PMYFFLYNLSFIDFCYSSVIT PKMLMSFVLKKNSISYAGC MTQLFFLFFVVSESFILSA MAYDRYVAICNPLLYMVT MSPQVCFLLLGVYGMGFA GAMAHTACMMGVTFCANN LVNHYMCDILPLLECACTST YVNELVVFVVVGIDIGVPT VTIFISYALILSSIFHIDSTEG RSKAFSTCSSHIIAVSLFFGS GAFMYLKPFSLLAMNQGKV SSLFYTVVPMLNPLIYSLR NKDVKVALKKILNKNAFS

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC006313_C	177/178	ACATGGAGAGACAAAGAATTATAGCAGCAGCACCTCAGGCTTCATCCTCCTGGGCCTC TCTTCCAACCCTAAGCTGCAGAAACCTCTCTTGCCATCTTCCTCATCATGTACCTAC TCACTGCGGTGGGGAATGTGCTCATCATCCTGCCCATCTACTCTGACCCCAGGCTCC ACACCCTATGTACTTTTTCTCAGCAACTTGTCTTTCATGGATATCTGCTTCACAAC AGTCATAGTGCCTAAGATGCTGGTGAATTTTCTATCAGAGACAAAGATTATCTCTTA TGTGGGCTGCCTGATCCAGATGTACTTCTTCATGGCATTTGGGAACACTGACAGCTA CCTGCTGGCCTCTATGGCCATCGACCGGCTGGTGGCCATCTGCAACCCCTTACACTA TGATGTGGTTATGAAACCATGGCATTGCCTACTCATGCTATTGGGTTCTTGCAGCAT CTCCCACCTACATTCCCTGTTCCGGTGCTACTTATGTCTCGCTTGTCTTTCTGTGCC TCTCACATCATTAAGCACTTTTCTGTGACACCCAGCCTGTGCTAAAGCTCTCCTGC TCTGACACATCCTCCAGCCAGATGGTGGTGATGAGACCTTAGCTGTCATTGTG ACCCCTTCCTGTGTACCATCTTCTCCTACCTGCAAATCATCGTCACTGTGCTCAGA ATCCCCTCTGCAGCCGGGAAGTGGAAGGCCTTCTCTACCTGGCTCCCACCTCACT GTAGTGGTCCTGTTCTATGGGAGTGTCATCTATGTCTATTTTAGGCCTCTGTCCATG TACTCAGTGATGAAGGGCCGGGTAGCCACTGTGAGGAACAAAGATATGAAAAAGGGGTTTGAAGA GCTGAACCCTTTCATCTACAGCCTGAGGAACAAAGATATGAAAAAGGGGTTTGAAGA AATTAAGACACAGAATTTACTCATAGAAAGAACAAAAT	METKNYSSSTSGFILLGLSS NPKLQKPLFAIFLIMYLLTA VGNVLIILAIYSDPRLHTPM YFFLSNLSFMDICFTTVIVPK MLVNFLSETKIISYVGCLIQ MYFFMAFGNTDSYLLASMA IDRLVAICNPLHYDVVMKP WHCLLMLLGSCSISHLHSLF RVLLMSRLSFCASHIIKHFFC DTQPVLKLSCSDTSSSQMV VMTETLAVIVTPFLCTIFSYL QIIVTVLRIPSAAGKWKAFS TCGSHLTVVLFYGSVIYV YFRPLSMYSVMKGRVATV MYTVVTPMLNPFIYSLRNK DMKRGLKLRHRIYS

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC006313_B	179/180	GGTCAAACTGCCCTTTACATCTCTCCCACTGCTTCTCCAAACCCTATCCAGGAAGTC CAGAGACACATGGAGATAAAGAACTACAGCAGCAGCACCTCAGGCTTCATCCTCCTGG GCCTCTCTTCCAACCCTCAGCTGCAGAAACCTCTCTTTGCCATCTTCCTCATCATGTA CCTGCTCGCTGCGGTGGGGAATGTGCTCATCATCCCGGCCATCTACTCTGACCCCAG GCTCCACACACCCTATGTACTTTTTTCTCAGCAACTGTCTTCTTCATGGATATCTGCTTC ACAACAGTCATAGTGCCTAAGATGCTGGTGAATTTTCTATCAGAGACAAAGGTTAT CTCCTATGTGGGCTGCCTGCCGCCCAGATGTACTTCTTTATGGCATTTGGGAACACTGA CAGCTACCTGCTGGCCCTCTATGGCCATCGACCGGCTGGTGGCCATCTGCAACCCCTT ACACTATGATGTGGTTATGAAACCACGGCATTGCCTGCTCATGCTATTGGGTTCTTG CAGCATCTCCCACCTACATTCCCGTTCCGCGTGCTACTTATGTCTGCGCTTGTCTTTC TGTGCCTCTCACATCATTAAGCACTTTTCTGTGACACCCAGCCTGCTAAAGCTC TCCTGCTCTGACACATCCTCCAGCCAGATGGTGGTACCAGCCAGATGACTGGTCACTGTGC ATTGTGACCCCTTCCTGTGTATCATCTTCTCCTACCTGCGAATCATGGTCACTGTGC TCAGAATCCCCTCTGCAGCCGGGAAGTGGAAGGCCTTCTCTACCCTGGTGGCTCCACC TCACTGCAGTAGCCCTTTTCTATGGGAGTATTATTTATGTCTATTTTATGGGACCGGGTAGCCACAGTTATGTACACAGTAGACAC CATGTACTCAGTGGTTAGGGACCGGGTAGCCACAGTTATGTACACAGTAGACAC CCATGCTGAACCCTTCATCTACAGCCTGAGGAACAAAGATATGAAGAGGGGTTTG AAGAAATTACAGGACAGAATTTACCGGTAAAAGGAACAAAATGTTG	METKNYSSSTSGFILLGLSS NPKLQKPLFAIFLIMYLLTA VGNVLILAIYSDPRLHTPM YFFLSNLSFMDICFTTVIVPK MLVNFLSETKIISYVGCLIQ MYFFMAFGNTDSYLLASMA IDRLVAICNPLHYDVVMKP WHCLLMLLGSCSISHLHSLF RVLLMSRLSFCASHIIKHFFC DTQPVLKLSCSDTSSSQMV VMTETLAVIVTPFLCTIFSYL QIIVTVLRIPSAAGKWKAFS TCGSHLTVVLFYGSVIYV YFRPLSMYSVMKGRVATV MYTVVTPMLNPFIYSLRNK DMKRGLKKLRHRIYS

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC009900_A	181/182	TCTGACTCCCACCTCCACACCCCCATGTACTTCTTCCTCTCCAACCTGTGCTGGGCTG ACATCAGTTTCACCTCGGCCACGGTTCCCAAGATGACGGTGGACATGCAGTCGCAT AGCAGAGTCATCTCTTATGCGGGCTGCCTGACACGGATGTCTTTCTTCGTCCTTTTT GCATGTATAGAAGACATGCTCCTGACTGTGATGGCCCAGGACTGCTTGTAGCCATC TGTCGCCCTCTGCACTACGCAGTCATCGTGAATCCTCACCTCTGTCTTCTTAGTTT TGGTGTCCTTTTCCTTAGCCTGTTGGATTCCCAGCTGCACAGTAAGATTGTGTTAC AATTCACCTTCTTCAAGAATGTGGAAATCTCTCATTTGTCTGTGAGCCATCTCAAT TTCTCAACCTTGCGTGTTCTGACAGCTTCATCAATAGCATATTCATGTATTTCGATA GTACTATGTTTGGTTTTCTTCCCATTTCAGGGATCCTTTGTCTTACTATAAAATTGT CCCCTCCATTCTAAGGGATTTCATCGTCAGATGGGAAGTATAAAGCCTTCTCCACCTG TGGCTCTCACCTGGCAGTTGTTTGCTTATTTTATGGAACAGGCATTGGCGTGTACCT GACTTCAGCTGTGGCACCACCCCCAGCAATGGTGTGGTGGCATCAGTGAAGTACA CCGTGGTCACCCCCATGCTGAACCCTTTCATCTACAGCCTGAGAAACAGGGACATTC AAAGCACCCTGTGGAGGCTGTGCAGCAGAACAGTTAAATCTTGATCTGTTCCATT CTTTTTCTGTGTGGGTAAGAAAGGGCAACCACAAAAAATCCCTACACATCTGCAAATC CTGCCCTTAGTCACATTATTTCGTGGCTGGATGGTTTATTCCTTTCCGCCATTTCCT ATGTGAATATTGTTTTCTTCTCGTTATGCCTTTAACTGGAATGGGGTGA	MYFFLSNLCWADISFTSATV PKMTVDMQSHSRVISYAGC LTRMSFFVLFACIEDMLLTV MAQDCFVAICRPLHYAVIV NPHLCVFLVLVSFFLSLLDS QLHSKIVLQFTFFKNVEISHF VCEPSQFLNLACSDSFINSIF MYFDSTMFGFLPISGILLSY YKIVPSILRISSSDGKYKAFS TCGSHLAVVCLFYGTGIGV YLTSAVAPPPSNGVVASVK YTVVTPMLNPFIYSLRNRDI QSTLWRLCSRTVKSLDLFHS FSCVGKKGQPQKIPTSANPA LSHIISVAGWFYSFPHFLCE YCFLRYAFNWNG

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC009545_B	183/184	CAATGGTGGGAAACCTCCTCATTTGGGTGACTACTATTGGCAGCCCCTCCTTGGGCT CCCTAATGTACTTCTTCCTTGCCTACTTGTCACTTATGGATGCCATATATTCCACTGC CATGTCACCCAAATTGATGATAGACTTACTCTGTGATAAAATCGCTATTTCCTTGTC AGCTTGCATGGTCAGCTCTTCATAGAACACTTACTTGGTGGTGCAGAGGTCTTCCT TTTGGTGGTGATGGCCTATGGCCTATCGCTATCTCTAAGCCGCTGCACTATTT GAACATCATGAATCGACTGGTTTGCATCCTTCGTTGGTGGTGGCCATGATTGGAGG TTTTGTGCACTCTGTGGTTCAAATTGTCTTTCTGTACAGTCTACCAATCGTGGCCCC AATGTTATTGACCACTCTGTCTGTGACATGTACCCATTGTTGGAACTGTTGTGCCTT GACACCTACTTTATAGGACTCACTGTGGTTGCCAATGGTGGAATAATTGTATGGTC ATCTTTACCTTTCCTGCTAATCTCCTGTGGAGTCATCCTAAACTTCCTTAAAACTTACA GTCAGGAAGAGAGGCATAAAGCCCTGCCTACCTGCCATCTCCCACATCATTGTGTT GCCCTCGTTTGTTCCCTGTATTTTATGTATGTTAGACCCGTTTCCAACTTTCCCT TTGATAAATTAATGACTGTGTTTTATTCAATTATCACACTCATGTTGAATCCTTTAAT ATACTCGTTGAGACAATCAGAGAATGAAAAATGCTATGAAAAATCTCTGGTGTGAAA AGTTAAGTATAGTTAGAAAAAGAGTATCTCCACACTGAACATATATTTATTCCTAGTT CTAAGGCAACAACAAATAGGCGGTAAAAATACTGCA	MVGNLLIWVTTIGSPSLGSL MYFFLAYLSLMDAIYSTAM SPKLMIDLLCDKIAISLSAC MGQLFIEHLLGGAEVFLLV VMAYDRYVAISKPLHYLNI MNRLVCILLVVAMIGGFV HSVVQIVFLYSLPICGPNVID HSVCDMYPLLELLCLDTYFI GLTVVANGGIICMVIFTFLLI SCGVILNFLKTYSQEERHKA LPTCISHIIVVALVFVPCIFM YVRPVSNFPFDKLMTVFYSI ITLMLNPLIYSLRQSEMKNA MKNLWCEKLSIVRKRVSPT LNIFIPSSKATNRR

180

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
CG56847-01	185/186	GCCCATGGGTAACTGGACTGCAGCGGTGACTGAGTTTGTTCTGCTGGGGTTTTCCCT GAGCGGGGAGGTGGAGCTGCTGCTCCTGGTGCTGCTGCCCACGTTCCTGCTGA CTCTTCTGGGGAACCTGCTCATCATCTCCACTGTGCTGTCCTCCCGCCTCCACA CCCCCATGTACTTCTTTGTGCAACCTCTCTATCCTGGACATCCTCTTCACCTCAGT CATCTCTCCAAAAGTGTTGGCCAACTTAGGATCTAGGGATAAAACCATCTCCTTTGC CGGATGTATCACCCAGTGCTATTTCTACTTTTTCTTGGGCACAGTTGAGTTCCTCCT GCTGACGGTCATGTCCTATGACCGTTATGCCACCATCTGCTGCCCCCTGCGGTACAC CACCATCATGAGACCTTCTGTCTGCATTGGGACCGTTGTATTCTCTTGGGTGGGAGG CTTCCTGTCTGTGCTCTTTCCAACCATCCTCATCTCCCAGCTGCCCTTCTGTGGCTCC AATATCATTAACCACTTCTTCTGTGACAGTGGACCCTGCTGGCCCTGGCCTGTGCA GACACCACTGCCCATCGAGCTGATGGATTTTATGCTTTCTTCCATGGCCTTGTTTGC TGCATAGTCCTCGTGGCCTATTCCTATACGTACATCATCTTGACCATAGTGCGGCATT CCTTTCTGCAAGTGGAAGGAAGGAAGAAGGCCTTTAATACCTGTGCTTCCCACTGACCATA GTCATCATTTCTAGTGGCATCACTGTGTTTATCTATGTGACTCCCTCCCAGAAAGAA TATCTGGAGATCAACAAGATCCCTTTGGTTCTGAGCAGTGGTGGTCACTCCTTCCTC AACCCCTTTATATATACTCTGAGGAATGACACAGTGCAGGGAGTCCTCAGGGATGT GTGGGTCAGGGTTCGAGGAGTTTTTGAAAAGAGGAAGGGCTTGCTCTTCTCCACCATGTGTC AGATTATCCTCCAACAAAGACCACCAAGGAAGGCCTTGCTCTTCTCCACCATGTGTC TATTCTGTAAAGCTCCAGTGTTAGAAAGAGAGGAGCTGCCTTA	MGNWTAAVTEFVLLGFSLS GEVELLLVLLLPTFLLTLL GNLLIISTVLSCSRLHTPMYF FLCNLSILDILFTSVISPKVLA NLGSRDKTISFAGCITQCYF YFFLGTVEFLLLTVMSYDR YATICCPLRYTTIMRPSVCIG TVVFSWVGGFLSVLFPTILIS QLPFCGSNIINHFFCDSGPLL ALACADTTAIELMDFMLSS MVILCCIVLVAYSYTYIILTI VRIPSASGRKKAFNTCASHL TIVIISSGITVFIYVTPSQKEY LEINKIPLVLSSVVTPFLNPFI YTLRNDTVQGVLRDVWVR VRGVFEKRMRAVLRSRLSS NKDHQGRACSSPPCVYSVK LQC

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
CG57811-01	187/188	CCCTCCTTGGGCTCCCTAATGTACTTCTTCCTTGCCTACTTGTCACTTATGGATGCCA TATATTCCACTGCCATGCCATGGTCACCCAAATTGATGATAGACTTACTCTGTGATAAAATCG CTATTTCCTTGTCAGCTTGCATGGGTCAGCTCTTCATAGAACACTTACTTGGTGGTG CAGAGGTCTTCCTTTGGTGGTGATGGCCTATGGCTATCTCTAAGC CGCTGCACTATTGAACATCATGAATGCGACTGGTTTGCATCCTTCGTTGGTGGTGG CCATGATTGGAGGTTTTGTGCACTCGTGGGTTCAAATTGTCTTTCTGTACAGTCTAC CAATCTGTGGCCCCAATGTTATTGACCACCTCTGTCGTGTGTGACATGTACCCATTGTTGG AACTGTTGTGCATTGACACCTACTTTATAGGACTCACTGTGGTTGCCAATGGTGGAACTT TAATTTGTATGGTCATCTTTACCTTTCTGCTAATCTCCTGTGGAGTCATCCTAAACTT CCTTAAAACTTACAGTCAGGAAGAGAGGCATAAAGCCCTGCCTACCTGCATCTCCC ACATCATTGTGGTTGCCCTCGTTTTGTTCCCTGTATTTTATGTATGTTAGACCCGT TTCCAACTTTCCCTTGATAAATTAATGACTGTGTTTATTCAATTATCACACTCATG TTGAATCCTTAATATACTCGTTGAGACAATCAGAGATGAAAAATGCTATGAAAAA TCTCTGGTGTGAAATGTTAAGTATAGTTAGAAAAAGAGTATCTCCCACACTGAACA TATTTATTCCTAGTTCTCAAGGCAACAAATAGGCGGTAAAATACTGCA	PSLGSLMYFFLAYLSLMDAI YSTAMSPKLMIDLLCDKIAI SLSACMGQLFIEHLLGGAEV FLLVMAYDRYVAISKPLH YLNIMNRLVCILLVVAMIG GFVHSVVQIVFLYSLPICGP NVIDHSVCDMYPLLELLCID TYFIGLTVVANGGIICMVIFT FLLISCGVILNFLKTYSQEER HKALPTCISHIIVVALVFVPC IFMYVRPVSNFPFDKLMTVF YSIITLMLNPLIYSLRQSEMK NAMKNLWCEMLSIVRKRV SPTLNIFIPSSKATNRR

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
SC88066175_A	189/190	GATGGTGTGGGAAAACCAGACCTTCAACTCCATCTTCATCCTGCTGGGAATCTTCAA TCACAGTCCCACCCACCTTCCTTTTTCTCGTGCTCGGCATCTTCTCACTGGCA TTGATGGAAAATATTTCCATGGTTCTCCTCATCTACATAGAGAAACAGCTCCACACC CCCATGTACTTCCTCCTCAGTCAACTGTCCCTTATGGACCTCATGTCATCTGCACC ACTCTACCCAAGATGATCTTCAGCTACTTGTCTGGGAAGAAATCTATCTCTCTGGCA GGTTGTGGAACTCAGATATTCTTCTATGTGTCCCGCTTGGAGCTGAATGTTTCTTG TTGGCTGTCATGGCTTATGACCGCTATATGTGGCTATATGTCACCCTCTTCAGTACACC ATCCTCATGAATCCGAAACTCTGTGTCTTCATGAGCTGTCGTCATTTCTTACTGCTTCC TCTCTTGATGGGATCATCACTTTTCTGTGATGTTGCTGCCCTTTACCTCTATCCTGCACAGA TGGAAATTCATCATCTTTTCTGAAAGACTACTTGTCATTGTTGTGGTAATGCTAATCTTTCC AACATCTGCATTTGAAAGACTACTTGTCATTGTTGTGGTAATGCTAATCTTTCC AGTTTCAGTTATCATACTTTCCATTCCCATGTCCTTGAGCCGTCATCCACATGG CTCTGGGGAAAGTCGTCGCAAGGCCTTCACTACCTGCTCCCCACCTGTCTGTGGT CGGACTCTACTACGGTGCTGCTATGTTCATGTACATGAGACCAGCTTCAAACATAC GCCAGACCAGGACAAGATGGTGTGGCCCAACAAAGAAGTGTTCAGGGCACTACAGAAGGTAC CCCTCTCATTTATAGCCTCCGCAACAAAGAAGTTAATATGACCTTATCAAAATCTTTTGA TGAAGAAAGAAAGTTAATATGACCTTATCAAAATCTTTTGA	MVWENQTFNSIFILLGIFNH SPTHTFLFSLVLGIFSLALME NISMVLLIYIEKQLHTPMYF LLSQLSLMDLMLICTTLPKM IFSYLSGKKSISLAGCGTQIF FYVSLLGAECFLLAVMAYD RYVAICHPLQYTILMNPKLC VFMTVASWTLGSLDGIIVLA AVLSFSYCSSLEIHHFFCDV AALLPLSCTETSAFERLLVIC CVVMLIFPVSVIILSYSHVLR AVIHMGSESRRKAFTTCSS HLSVVGLYYGAAMFMYMR PASKHTPDQDKMVSAFYTI LTPMLNPLIYSLRNKEVFRA LQKVLKKRKLI

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Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMba245d2_C	191/192	GCATATTCATCATGGCATGGGAGAATCAGAGACCTTCAACTCTGACTTCCTCCTCCTGG GAATCTTCAATCATAGCCCACCCACCACCTTCCTCTTCTTTCTGGTCCTGGCCATCTT TTCAGTGGCCTTCATGGGAAACTCCATCATGGTTCTCCTCATCTACCTGGATACCCA GCTCCACACCCCAATGTACTTCCTCCTCAGCCAACTGTCCCTCATGGACCTCATGCT CATCTGCACCACTGTACCCAAGATGGCCTTCAACTACTTCTCTTCTATATATCATTGCTTGGCTCCGA ATGCTTTCTGTTGGCTGTTATGTCTTATGACCGCTACACTGCCATTTGCCACCCTCTA AGATACACCAATCTCATGAGACCCAAAATTTGTGGACTTATGACTGCCTTCTCCTGG ATCCTGGGCTCTACAGATGGAATCATTGATGCTGTAGGCGACATTTCCTTCTCCTAC TGTGGGTCTCGGGAAATAGCCCACTTCTGCTGCTGACTTCCCCTACTAATCCTC TCATGCAATGACACATCAATATTGAAGAGGTTATTTCATCGCTGTATAGTAATG CTTGTTTCCCGTTGCAATCATCATCACTTCCTATGCTCGAGTTATTCTGGCTGTCA TTCACATGGGATCTGGAGAGGAGGACGTCGCAAAGCTTTTACTACTTGTTCCTCTCACC TCATGGTGGTGGGAATGTACTATGGAGCAGGTTTGTTCATGTGCATTCAGCCCACAT CTCATCATTCTCCTATGCAGGACAAGATGGTGTCGTATTCTACACCATCGTCACTC CCATGCTGAATCCTCTCATTTATAGCCTCCGCAACAAGGAAGTGACCAGAGCATTA ATGAAAATCTTAGGAAAGGGCAAGTCTGGAGATTGA	MAWENQTFNSDFLLLGIFN HSPTHTFLFFLVLAIFSVAF MGNSIMVLLIYLDTQLHTP MYFLLSQLSLMDLMLICTT VPKMAFNYLSGSKSISMAG CATQIFFYISLLGSECFLLAV MSYDRYTAICHPLRYTNLM RPKICGLMTAFSWILGSTDG IIDAVATFSFSYCGSREIAHF CCDFPSLLILSCNDTSIFEEVI FICCIVMLVFPVAIIITSYAR VILAVIHMGSGEGRRKAFTT CSSHLMVVGMYYGAGLFM CIQPTSHHSPMQDKMVSVF YTIVTPMLNPLIYSLRNKEV TRALMKILGKGKSGD

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMba245d2_A	193/194	GGGAAATTATGGAGAGATGAGAAATACTACCACCCCAGATTTTATTCTCCTAGGACTCTTTA ACCACACAGGAGCCCACCAAGTCCTCTTCATGATGCTTCTGGCCACCGTTTTGACCT CCCTGTTTAGCAATGCCCTCATGATTCTCCTGATTCACTGGGACCACCGGCTCCACA GGCCCATGTACTTCCTGAGCCAACTTCCCTCATGGACATGATGCTGGTTTCCA CCACTGTGCCAAAATGGCGGCTGACTACTTGACCGGAAATAAGGCCATCTCCCGC GCTGGCTGGTGGTGCAGATCTTCTTCTTCCTCCCCACACTGGGTGGTGGAGAGTGCTTC CTCTTAGCAGCCATGGCCTATGACCGGCTATGCGGCTGTCTGCCACCCACTCCGATAT CCCACTTCTCATGAGCTGGCAGCTGGCCTGTGCCTGAGGATGACCATGTCGTCCTGGCTCCTG GGTGCAGCTGACGGCCTCCTGCAGGCTGTTGCTACCCTGAGCTTCCCATATTGCGGT GCACACGAGATGATCACTTCTTCTGCGAGGCCCCCGTGTTGGTGGCTTGT GCTGACACTTCAGTCTTCGAAAACGCCATGTACATCTGCGTGTTGTTAATGCTCCTG GTCCCCTTTCCCTCATCCGTGTCCTCCTATGGTCTCATCCTCCGCGTCGTTCTGCTCA TGCGCTCTACAGAAGCCCGCAAGAAGGCCTTTGCCACCTGCTCTTCACATGTGGCTG TGGTGGGACTCTTTTATGGAGCTGCCATTTTTACCTATATGAGACCCAAATCCCATA GGTCCACTAACCATGACAAGGTTGTGTCAGCCTTCTATACTATGTTCACCCCTTTAC TAAACCCCCTCATCTACCACGTGTAAACATAAAAACACCAGCAAATGAGGCCCACAGGTCAAG TGGCTGGGGACGTGTGTAAACATAAAAACACCAGCAAATGAGGCCCACAGGTCAAG ATGATCTAAT	MEMRNTTPDFILLGLFNHT RAHQVLFMLLATVLTSLF SNALMILLIHWDHRLHRPM YFLLSQLSLMDMMLVSTTV PKMAADYLTGNKAISRAGC GVQIFFLPTLGGGECFLLAA MAYDRYAAVCHPLRYPTL MSWQLCLRMTMSSWLLGA ADGLLQAVATLSFPYCGAH EIDHFFCEAPVLVRLACADT SVFENAMYICCVLMLLVPFS LILSSYGLILAAVLLMRSTE ARKKAFATCSSHVAVVGLF YGAAIFTYMRPKSHRSTNH DKVVSAFYTMFTPLLNPLIY SVKNSEVKGALKRWLGTC VNIKHQQNEAHRSR

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
CG92751-01	195/196	CACTGGAGAGATTCTCCTCTGTGGACTTTTCTCTGCCTTCTATACACTCACCCTGCTGGG GAATGGGGTCATCTTTGGGATTATCTGCCTGGACTGTAAGCTTCACACACCATGTA CTTCTTCCTCTCACACCTGGCCATTGTTGACATATCCTATGCTTCCAACTATGTCCCC AAGATGCTGACGAATCTTATGAACCAGGAAAGCACCATCTCCTTTTTTCCATGCATA ATGCAGACATTCTTGTATTTGGCTTTTGCTCACGTAGAGTGTCTGATTTGGTGGTG ATGTCCTATGATCGCTATGCGGACATCTGCCACCCTTACGTTACAATAGCCTCATG AGCTGGAGAGTGTGCACTGTCTCCTGGCTGTGGCTTCCTGGGTGTTCAGCTTCCTCTG GCTCTGGTCCCTTTAGTTCTCATCCTGTGTGAAATCCTGTCTGTCCTCAAGTTGGCCTGG AACCACTTCTTCTGTGAAATCCTGTCTGTCCTCAAGTTGGCCTGG CTCAACCAGGTGGTCATCTTTGCAGCCTGCGTGTTCATCCTGGTGGGGCCACTCTGC CTGGTGCTGGTCTCCTACTTGCGCATCCTGGCCGGCATCTTGAGGATCCAGTCTGGG GAGGGCCGCAGAAAGGCCTTCTCCACCTGCTCCTCCCACCTTTGCGTGGTGGGGACTC TTCTTTGGCAGCGCCATTGTCACGTACATGGCCCCCAAGTCCCGCCATCCTGAGGAG CAGCAGAAAGTTCTTTCCCTGTTTTACAGCCTTTCAATCCAATGCTGAACCCCCTG ATATATAGCCTAAGGAATGCAGAGGTCAAGGGCGCCCTGAGGAGGGCACTGAGGA AGGAGAGGCTGACGTGAGACATCTCAAAG	LEILLCGLFSAFYTLTLLGN GVIFGIICLDCKLHTPMYFFL SHLAIVDISYASNYVPKMLT NLMNQESTISFFPCIMQTFL YLAFAHVECLILVVMSYDR YADICHPLRYNSLMSWRVC TVLAVASWVFSFLLALVPL VLILSLPFCGPHEINHFFCEIL SVLKLACADTWLNQVVIFA ACVFILVGPLCLVLVSYLRIL AAILRIQSGEGRRKAFSTCSS HLCVVGLFFGSAIVTYMAP KSRHPEEQQKVLSLFYSLFN PMLNPLIYSLRNAEVKGALR RALRKERLT

Table 1

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
CG59943-01	197/198	GATGGTGTGGGAAAACCAGACCTTCAACTCCATCTTCATCCTGCTGGAATCTTCAATCACAGTCCCACCCACCTTCCTTTTTCTCGGTCCTGGGCATCTTCTCACTGGCATTGATGGAAAATATTTCCATGGTTCTCCTCCATCTCACATAGAGAAACAGCTCCACACCCCCATGTACTTCCTCCTCAGTCAACTGTCCCTTATGGACCTCAACTGCTCATCTGCACCACTCTACCCAAGATGATCTTCAGCTACTACTTGTCTGGGAAGAAATCTATCTCTGGCAGGTTGTGGAACTCAGATATTCTTCTATGTGTCCCTGCTTGGAGCTGAATGTTTCTTGTTGGCTGTCATGGCTTATGACCGGCTATGTGCTATATGTGGCTATATGTGTCACCCTCTTCAGTACACCATCCTCATGAATCCGAAACTCTGTGTCTTCATGACTGTTGCTTGCAGCTGTCCTGTCGTCCTGTCATTTCTTCTTACTGCAGCTCTCTCTCTTGATGGGATCATAGTGCTTGCAGCTGTCCTGTCGTCCTGTCATTTCTTCTTACTGCAGCTCTCTGGAAATTCATCATTTTTCTGTGATGTTGCTGCCCCTTTACCTCTATCCCGCACAGAAACATCTGCATTTGAAAGACTACTTGTCATTGTGTGTGGTAATGCTAATCTTTCCAGTTTCAGTTATCATACTTTCCTATTCCCATGTCCTTCGAGCGGTCATCCACATGGGCTCTGGGGAAAGTCGTCGCAAGGCCTTCACTACCTGCTCCTCCCACCTGTCTCTGGTCGGACTCTACTACGGTGCTGCTATGTTCATGTACATGAGACCAGCCAGTCATCTCCCCATTCAGCCTTACGGTGCTGCTATGTTCATGTACATGAGACCAGCCAGTCATCTCCCCATTCAGCCTTACGGTGCTGCTATGTTCATGTACATGAGACCAGCCAGGCTCGGCCTTCACCCCTATGCTGAAGCCAGACCAGGACAAGATGGTGTCGGCCTTCACCCCTATGCTGAAGCCAGACCAGGACAAGATGGTGTCGGCCTTTATAGCCTCCGCAACAAGAAGTGTTCAGGGCACTACAGAAGGTACCCCTCTCATTTATAGCCTCCGCAACAAGAAGTGTTCAGGGCACTACAGAAGGTACTGAAGAAAGAAAGTTAATATGACCTTATCAAAATCTTTTGA	MVWENQTFNSIFILLGIFNH SPTHTFLFSLVLGIFSLALME NISMVLLIYIEKQLHTPMYF LLSQLSLMDLMLICTTLPKM IFSYLSGKKSISLAGCGTQIF FYVSLLGAECFLLAVMAYD RYVAICHPLQYTILMNPKLC VFMTVASWTLGSLDGIIVLA AVLSFSYCSSLEIHHFFCDV AALLPLSRTETSAFERLLVIC CVVMLIFPVSVIILSYSHVLR AVIHMGSGESRRKAFTTCSS HLSVVGLYYGAAMFMYMR PASKHTPDQDKMVSAFYTI LTPMLNPLIYSLRNKEVFRA LQKVLKKRKLI

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Table 1

Acc. No.	SEQ ID NO (Nucl)/ SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP001804_B _1	199/200	TTAATGGCTGTGGAAAAATGACTCTTCAGGGACAAGAGTTTATTCTTTTGGGATTAAC AGACCAGCCTGAGATCCAATTGCCCCCTGTTTTTCCTGTTCTTGGTGAACTATATGAC CACCATGGTGGGCAACTTGAGTTAATTAATCTAATTTGCCTGAATTCACACCTTCA CACTCCCATGTATTTTTCCTTTCAATCTGTCCTTCATTGATCTCTGTTATTCATTTG TCTTTACCCCCAAAATGCTGATGAGCTTTATTTCAGAGAGGAACATCATCTCCTTTC CAGGATGCATAACTCAGCTCTTTTTCTTCTGCTTTTTTGTCCACTCTGAGTGCTATGT GCTGACAGCCATGGCCTATGATCGGCTATGTGGCCATCTGCAAACCCCTTCGTACAT GGTCACCACGTCCCCTCAGATCTGTTCTCTACTGATGCTTGGTTCATATGTGATGGG GTTTGCTGGGGCCATGGTCCACACAGAGTGTATGATGAAGCTCATCTTTTGTGACTC CAACGTCATCAACCATTACATGTGTGACATCTTCCCACTGCTCCTCCTGCAG CAGCACCCAGGCCAATGAGCTGGTGATGTCGTTATTGTAGGCACAGTTGTTATAGT ATCAAGCCTCATTATCTTAATCTCTTATGCTTTGATTCTTTTCAATATCCTTCACATG TCCTCAGCCGAGGGTTGGTTCAAAGCCATGGCCATCCGTACCGTGGCTCCCACATAATAACT GTTGGCCTATTCTATGAATTTGGGCTGATCACTCATGTTAAGTTATCATCTGATTGG TATATGGGTCAGGGGAAGTTTCTCCAGTGTTTTACACGAATGGTGTACCCATGCTG AACCCCCTCATTTATAGCCTCAGGAACAAGGATGTCAAACTTGCTCTAAAGGAAAC CCTAAATAAAATTACAAACTGA	MLARNNSLVTEFILAGLTD HPEFQQPLFLFLVVYIVTM VGNLGLILFGLNSHLHTPM YYFLFNLSFIDLCYSSVFTPK MLMNFVSKKNIISYVGCMT QLFFLFFVISECYMLTSMA YDRYVAICNPLLYKVTMSH QVCSMLTFAAYIMGLAGAT AHTGCMLRLTFCSANIINHY LCDILPLLQLSCTSTYVNEV VVLIVVGINIMVPSCTILISY VFIVTSILHIKSTQGRSKAFS TCSSHVIALSLFFGSAAFMYI KYSSGSMEQGKVSSVFYTN VVPMLNPLIYSLRNKDVKV ALRKALIKIQRRNIF

Example 1: Quantitative expression analysis of clones in various cells and tissues

The quantitative expression of various clones was assessed using microtiter plates
5   containing RNA samples from a variety of normal and pathology-derived cells, cell lines and
tissues using real time quantitative PCR (RTQ PCR). RTQ PCR was performed on an
Applied Biosystems ABI PRISM® 7700 or an ABI PRISM® 7900 HT Sequence Detection
System. Various collections of samples are assembled on the plates, and referred to as Panel
1 (containing normal tissues and cancer cell lines), Panel 2 (containing samples derived from
10   tissues from normal and cancer sources), Panel 3 (containing cancer cell lines), Panel 4
(containing cells and cell lines from normal tissues and cells related to inflammatory
conditions), Panel 5D/5I (containing human tissues and cell lines with an emphasis on
metabolic diseases), AI_comprehensive_panel (containing normal tissue and samples from
autoimmune diseases), Panel CNSD.01 (containing central nervous system samples from
15   normal and diseased brains) and CNS_neurodegeneration_panel (containing samples from
normal and Alzheimer's diseased brains).

RNA integrity from all samples is controlled for quality by visual assessment of
agarose gel electropherograms using 28S and 18S ribosomal RNA staining intensity ratio as a
guide (2:1 to 2.5:1 28s:18s) and the absence of low molecular weight RNAs that would be
20   indicative of degradation products. Samples are controlled against genomic DNA
contamination by RTQ PCR reactions run in the absence of reverse transcriptase using probe
and primer sets designed to amplify across the span of a single exon.

First, the RNA samples were normalized to reference nucleic acids such as
constitutively expressed genes (for example, β-actin and GAPDH). Normalized RNA (5 ul)
25   was converted to cDNA and analyzed by RTQ-PCR using One Step RT-PCR Master Mix
Reagents (Applied Biosystems; Catalog No. 4309169) and gene-specific primers according to
the manufacturer's instructions.

In other cases, non-normalized RNA samples were converted to single strand cDNA
(sscDNA) using Superscript II (Invitrogen Corporation; Catalog No. 18064-147) and random
30   hexamers according to the manufacturer's instructions. Reactions containing up to 10 μg of
total RNA were performed in a volume of 20 μl and incubated for 60 minutes at 42°C. This

reaction can be scaled up to 50 µg of total RNA in a final volume of 100 µl. sscDNA samples are then normalized to reference nucleic acids as described previously, using 1X TaqMan® Universal Master mix (Applied Biosystems; catalog No. 4324020), following the manufacturer's instructions.

5   Probes and primers were designed for each assay according to Applied Biosystems Primer Express Software package (version I for Apple Computer's Macintosh Power PC) or a similar algorithm using the target sequence as input. Default settings were used for reaction conditions and the following parameters were set before selecting primers: primer concentration = 250 nM, primer melting temperature (Tm) range = 58°-60°C, primer optimal

10   Tm = 59°C, maximum primer difference = 2°C, probe does not have 5'G, probe Tm must be 10°C greater than primer Tm, amplicon size 75bp to 100bp. The probes and primers selected (see below) were synthesized by Synthegen (Houston, TX, USA). Probes were double purified by HPLC to remove uncoupled dye and evaluated by mass spectroscopy to verify coupling of reporter and quencher dyes to the 5' and 3' ends of the probe, respectively. Their

15   final concentrations were: forward and reverse primers, 900nM each, and probe, 200nM.

PCR conditions: When working with RNA samples, normalized RNA from each tissue and each cell line was spotted in each well of either a 96 well or a 384-well PCR plate (Applied Biosystems). PCR cocktails included either a single gene specific probe and primers set, or two multiplexed probe and primers sets (a set specific for the target clone and another

20   gene-specific set multiplexed with the target probe). PCR reactions were set up using TaqMan® One-Step RT-PCR Master Mix (Applied Biosystems, Catalog No. 4313803) following manufacturer's instructions. Reverse transcription was performed at 48°C for 30 minutes followed by amplification/PCR cycles as follows: 95°C 10 min, then 40 cycles of 95°C for 15 seconds, 60°C for 1 minute. Results were recorded as CT values (cycle at which a

25   given sample crosses a threshold level of fluorescence) using a log scale, with the difference in RNA concentration between a given sample and the sample with the lowest CT value being represented as 2 to the power of delta CT. The percent relative expression is then obtained by taking the reciprocal of this RNA difference and multiplying by 100.

When working with sscDNA samples, normalized sscDNA was used as described

30   previously for RNA samples. PCR reactions containing one or two sets of probe and primers were set up as described previously, using 1X TaqMan® Universal Master mix (Applied

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Biosystems; catalog No. 4324020), following the manufacturer's instructions. PCR amplification was performed as follows: 95°C 10 min, then 40 cycles of 95°C for 15 seconds, 60°C for 1 minute. Results were analyzed and processed as described previously.

Panels 1, 1.1, 1.2, and 1.3D

5   The plates for Panels 1, 1.1, 1.2 and 1.3D include 2 control wells (genomic DNA control and chemistry control) and 94 wells containing cDNA from various samples. The samples in these panels are broken into 2 classes: samples derived from cultured cell lines and samples derived from primary normal tissues. The cell lines are derived from cancers of the following types: lung cancer, breast cancer, melanoma, colon cancer, prostate cancer,

10   CNS cancer, squamous cell carcinoma, ovarian cancer, liver cancer, renal cancer, gastric cancer and pancreatic cancer. Cell lines used in these panels are widely available through the American Type Culture Collection (ATCC), a repository for cultured cell lines, and were cultured using the conditions recommended by the ATCC. The normal tissues found on these panels are comprised of samples derived from all major organ systems from single adult

15   individuals or fetuses. These samples are derived from the following organs: adult skeletal muscle, fetal skeletal muscle, adult heart, fetal heart, adult kidney, fetal kidney, adult liver, fetal liver, adult lung, fetal lung, various regions of the brain, the spleen, bone marrow, lymph node, pancreas, salivary gland, pituitary gland, adrenal gland, spinal cord, thymus, stomach, small intestine, colon, bladder, trachea, breast, ovary, uterus, placenta, prostate, testis and

20   adipose.

In the results for Panels 1, 1.1, 1.2 and 1.3D, the following abbreviations are used:

ca. = carcinoma,

* = established from metastasis,

met = metastasis,

25   s cell var = small cell variant,

non-s = non-sm = non-small,

squam = squamous,

pl. eff = pl effusion = pleural effusion,

glio = glioma,

30   astro = astrocytoma, and

neuro = neuroblastoma.

General_screening_panel_v1.4

The plates for Panel 1.4 include 2 control wells (genomic DNA control and chemistry control) and 94 wells containing cDNA from various samples. The samples in Panel 1.4 are broken into 2 classes: samples derived from cultured cell lines and samples derived from primary normal tissues. The cell lines are derived from cancers of the following types: lung cancer, breast cancer, melanoma, colon cancer, prostate cancer, CNS cancer, squamous cell carcinoma, ovarian cancer, liver cancer, renal cancer, gastric cancer and pancreatic cancer. Cell lines used in Panel 1.4 are widely available through the American Type Culture Collection (ATCC), a repository for cultured cell lines, and were cultured using the conditions recommended by the ATCC. The normal tissues found on Panel 1.4 are comprised of pools of samples derived from all major organ systems from 2 to 5 different adult individuals or fetuses. These samples are derived from the following organs: adult skeletal muscle, fetal skeletal muscle, adult heart, fetal heart, adult kidney, fetal kidney, adult liver, fetal liver, adult lung, fetal lung, various regions of the brain, the spleen, bone marrow, lymph node, pancreas, salivary gland, pituitary gland, adrenal gland, spinal cord, thymus, stomach, small intestine, colon, bladder, trachea, breast, ovary, uterus, placenta, prostate, testis and adipose. Abbreviations are as described for Panels 1, 1.1, 1.2, and 1.3D.

Panels 2D and 2.2

The plates for Panels 2D and 2.2 generally include 2 control wells and 94 test samples composed of RNA or cDNA isolated from human tissue procured by surgeons working in close cooperation with the National Cancer Institute's Cooperative Human Tissue Network (CHTN) or the National Disease Research Initiative (NDRI). The tissues are derived from human malignancies and in cases where indicated many malignant tissues have "matched margins" obtained from noncancerous tissue just adjacent to the tumor. These are termed normal adjacent tissues and are denoted "NAT" in the results below. The tumor tissue and the "matched margins" are evaluated by two independent pathologists (the surgical pathologists and again by a pathologist at NDRI or CHTN). This analysis provides a gross histopathological assessment of tumor differentiation grade. Moreover, most samples include the original surgical pathology report that provides information regarding the clinical stage of the patient. These matched margins are taken from the tissue surrounding (i.e. immediately proximal) to the zone of surgery (designated "NAT", for normal adjacent tissue, in Table RR). In addition, RNA and cDNA samples were obtained from various human tissues derived

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from autopsies performed on elderly people or sudden death victims (accidents, etc.). These tissues were ascertained to be free of disease and were purchased from various commercial sources such as Clontech (Palo Alto, CA), Research Genetics, and Invitrogen.

Panel 3D

5   The plates of Panel 3D are comprised of 94 cDNA samples and two control samples. Specifically, 92 of these samples are derived from cultured human cancer cell lines, 2 samples of human primary cerebellar tissue and 2 controls. The human cell lines are generally obtained from ATCC (American Type Culture Collection), NCI or the German tumor cell bank and fall into the following tissue groups: Squamous cell carcinoma of the

10   tongue, breast cancer, prostate cancer, melanoma, epidermoid carcinoma, sarcomas, bladder carcinomas,   pancreatic   cancers,   kidney   cancers,   leukemias/lymphomas, ovarian/uterine/cervical, gastric, colon, lung and CNS cancer cell lines. In addition, there are two independent samples of cerebellum. These cells are all cultured under standard recommended conditions and RNA extracted using the standard procedures. The cell lines in

15   panel 3D and 1.3D are of the most common cell lines used in the scientific literature.

Panels 4D, 4R, and 4.1D

Panel 4 includes samples on a 96 well plate (2 control wells, 94 test samples) composed of RNA (Panel 4R) or cDNA (Panels 4D/4.1D) isolated from various human cell lines or tissues related to inflammatory conditions. Total RNA from control normal tissues

20   such as colon and lung (Stratagene, La Jolla, CA) and thymus and kidney (Clontech) was employed. Total RNA from liver tissue from cirrhosis patients and kidney from lupus patients was obtained from BioChain (Biochain Institute, Inc., Hayward, CA). Intestinal tissue for RNA preparation from patients diagnosed as having Crohn's disease and ulcerative colitis was obtained from the National Disease Research Interchange (NDRI) (Philadelphia, PA).

25   Astrocytes, lung fibroblasts, dermal fibroblasts, coronary artery smooth muscle cells, small airway epithelium, bronchial epithelium, microvascular dermal endothelial cells, microvascular lung endothelial cells, human pulmonary aortic endothelial cells, human umbilical vein endothelial cells were all purchased from Clonetics (Walkersville, MD) and grown in the media supplied for these cell types by Clonetics. These primary cell types were

30   activated with various cytokines or combinations of cytokines for 6 and/or 12-14 hours, as

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indicated. The following cytokines were used; IL-1 beta at approximately 1-5ng/ml, TNF alpha at approximately 5-10ng/ml, IFN gamma at approximately 20-50ng/ml, IL-4 at approximately 5-10ng/ml, IL-9 at approximately 5-10ng/ml, IL-13 at approximately 5-10ng/ml. Endothelial cells were sometimes starved for various times by culture in the basal

5   media from Clonetics with 0.1% serum.

Mononuclear cells were prepared from blood of employees at CuraGen Corporation, using Ficoll. LAK cells were prepared from these cells by culture in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco/Life Technologies, Rockville, MD), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), and 10mM Hepes

10   (Gibco) and Interleukin 2 for 4-6 days. Cells were then either activated with 10-20ng/ml PMA and 1-2μg/ml ionomycin, IL-12 at 5-10ng/ml, IFN gamma at 20-50ng/ml and IL-18 at 5-10ng/ml for 6 hours. In some cases, mononuclear cells were cultured for 4-5 days in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), and 10mM Hepes (Gibco) with PHA

15   (phytohemagglutinin) or PWM (pokeweed mitogen) at approximately 5μg/ml. Samples were taken at 24, 48 and 72 hours for RNA preparation. MLR (mixed lymphocyte reaction) samples were obtained by taking blood from two donors, isolating the mononuclear cells using Ficoll and mixing the isolated mononuclear cells 1:1 at a final concentration of approximately 2×10^{6}cells/ml in DMEM 5% FCS (Hyclone), 100μM non essential amino

20   acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol (5.5×10^{-5}M) (Gibco), and 10mM Hepes (Gibco). The MLR was cultured and samples taken at various time points ranging from 1- 7 days for RNA preparation.

Monocytes were isolated from mononuclear cells using CD14 Miltenyi Beads, +ve VS selection columns and a Vario Magnet according to the manufacturer's instructions.

25   Monocytes were differentiated into dendritic cells by culture in DMEM 5% fetal calf serum (FCS) (Hyclone, Logan, UT), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), and 10mM Hepes (Gibco), 50ng/ml GMCSF and 5ng/ml IL-4 for 5-7 days. Macrophages were prepared by culture of monocytes for 5-7 days in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM

30   sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), 10mM Hepes (Gibco) and 10% AB Human Serum or MCSF at approximately 50ng/ml. Monocytes, macrophages and dendritic cells were stimulated for 6 and 12-14 hours with lipopolysaccharide (LPS) at

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100ng/ml. Dendritic cells were also stimulated with anti-CD40 monoclonal antibody (Pharmingen) at 10μg/ml for 6 and 12-14 hours.

CD4 lymphocytes, CD8 lymphocytes and NK cells were also isolated from mononuclear cells using CD4, CD8 and CD56 Miltenyi beads, positive VS selection columns and a Vario Magnet according to the manufacturer's instructions. CD45RA and CD45RO CD4 lymphocytes were isolated by depleting mononuclear cells of CD8, CD56, CD14 and CD19 cells using CD8, CD56, CD14 and CD19 Miltenyi beads and positive selection. CD45RO beads were then used to isolate the CD45RO CD4 lymphocytes with the remaining cells being CD45RA CD4 lymphocytes. CD45RA CD4, CD45RO CD4 and CD8 lymphocytes were placed in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), and 10mM Hepes (Gibco) and plated at 10^6cells/ml onto Falcon 6 well tissue culture plates that had been coated overnight with 0.5μg/ml anti-CD28 (Pharmingen) and 3ug/ml anti-CD3 (OKT3, ATCC) in PBS. After 6 and 24 hours, the cells were harvested for RNA preparation. To prepare chronically activated CD8 lymphocytes, we activated the isolated CD8 lymphocytes for 4 days on anti-CD28 and anti-CD3 coated plates and then harvested the cells and expanded them in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), and 10mM Hepes (Gibco) and IL-2. The expanded CD8 cells were then activated again with plate bound anti-CD3 and anti-CD28 for 4 days and expanded as before. RNA was isolated 6 and 24 hours after the second activation and after 4 days of the second expansion culture. The isolated NK cells were cultured in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), and 10mM Hepes (Gibco) and IL-2 for 4-6 days before RNA was prepared.

To obtain B cells, tonsils were procured from NDRI. The tonsil was cut up with sterile dissecting scissors and then passed through a sieve. Tonsil cells were then spun down and resupended at 10^6cells/ml in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), and 10mM Hepes (Gibco). To activate the cells, we used PWM at 5μg/ml or anti-CD40 (Pharmingen) at approximately 10μg/ml and IL-4 at 5-10ng/ml. Cells were harvested for RNA preparation at 24,48 and 72 hours.

To prepare the primary and secondary Th1/Th2 and Tr1 cells, six-well Falcon plates were coated overnight with 10μg/ml anti-CD28 (Pharmingen) and 2μg/ml OKT3 (ATCC), and then washed twice with PBS. Umbilical cord blood CD4 lymphocytes (Poietic Systems, German Town, MD) were cultured at 10^5-10^6cells/ml in DMEM 5% FCS (Hyclone), 100μM

5   non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), 10mM Hepes (Gibco) and IL-2 (4ng/ml). IL-12 (5ng/ml) and anti-IL4 (1μg/ml) were used to direct to Th1, while IL-4 (5ng/ml) and anti-IFN gamma (1μg/ml) were used to direct to Th2 and IL-10 at 5ng/ml was used to direct to Tr1. After 4-5 days, the activated Th1, Th2 and Tr1 lymphocytes were washed once in DMEM and expanded for 4-7 days in DMEM

10   5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), 10mM Hepes (Gibco) and IL-2 (1ng/ml). Following this, the activated Th1, Th2 and Tr1 lymphocytes were re-stimulated for 5 days with anti-CD28/OKT3 and cytokines as described above, but with the addition of anti-CD95L (1μg/ml) to prevent apoptosis. After 4-5 days, the Th1, Th2 and Tr1 lymphocytes

15   were washed and then expanded again with IL-2 for 4-7 days. Activated Th1 and Th2 lymphocytes were maintained in this way for a maximum of three cycles. RNA was prepared from primary and secondary Th1, Th2 and Tr1 after 6 and 24 hours following the second and third activations with plate bound anti-CD3 and anti-CD28 mAbs and 4 days into the second and third expansion cultures in Interleukin 2.

20   The following leukocyte cells lines were obtained from the ATCC: Ramos, EOL-1, KU-812. EOL cells were further differentiated by culture in 0.1mM dbcAMP at 5×10^5cells/ml for 8 days, changing the media every 3 days and adjusting the cell concentration to 5×10^5cells/ml. For the culture of these cells, we used DMEM or RPMI (as recommended by the ATCC), with the addition of 5% FCS (Hyclone), 100μM non essential

25   amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), 10mM Hepes (Gibco). RNA was either prepared from resting cells or cells activated with PMA at 10ng/ml and ionomycin at 1μg/ml for 6 and 14 hours. Keratinocyte line CCD106 and an airway epithelial tumor line NCI-H292 were also obtained from the ATCC. Both were cultured in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM

30   sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5}M (Gibco), and 10mM Hepes (Gibco). CCD1106 cells were activated for 6 and 14 hours with approximately 5 ng/ml TNF alpha and

1ng/ml IL-1 beta, while NCI-H292 cells were activated for 6 and 14 hours with the following cytokines: 5ng/ml IL-4, 5ng/ml IL-9, 5ng/ml IL-13 and 25ng/ml IFN gamma.

For these cell lines and blood cells, RNA was prepared by lysing approximately 10^7cells/ml using Trizol (Gibco BRL). Briefly, 1/10 volume of bromochloropropane (Molecular Research Corporation) was added to the RNA sample, vortexed and after 10 minutes at room temperature, the tubes were spun at 14,000 rpm in a Sorvall SS34 rotor. The aqueous phase was removed and placed in a 15ml Falcon Tube. An equal volume of isopropanol was added and left at -20°C overnight. The precipitated RNA was spun down at 9,000 rpm for 15 min in a Sorvall SS34 rotor and washed in 70% ethanol. The pellet was redissolved in 300µl of RNAse-free water and 35µl buffer (Promega) 5µl DTT, 7µl RNAsin and 8µl DNAse were added. The tube was incubated at 37°C for 30 minutes to remove contaminating genomic DNA, extracted once with phenol chloroform and re-precipitated with 1/10 volume of 3M sodium acetate and 2 volumes of 100% ethanol. The RNA was spun down and placed in RNAse free water. RNA was stored at -80°C.

AI_comprehensive panel_v1.0

The plates for AI_comprehensive panel_v1.0 include two control wells and 89 test samples comprised of cDNA isolated from surgical and postmortem human tissues obtained from the Backus Hospital and Clinomics (Frederick, MD). Total RNA was extracted from tissue samples from the Backus Hospital in the Facility at CuraGen. Total RNA from other tissues was obtained from Clinomics.

Joint tissues including synovial fluid, synovium, bone and cartilage were obtained from patients undergoing total knee or hip replacement surgery at the Backus Hospital. Tissue samples were immediately snap frozen in liquid nitrogen to ensure that isolated RNA was of optimal quality and not degraded. Additional samples of osteoarthritis and rheumatoid arthritis joint tissues were obtained from Clinomics. Normal control tissues were supplied by Clinomics and were obtained during autopsy of trauma victims.

Surgical specimens of psoriatic tissues and adjacent matched tissues were provided as total RNA by Clinomics. Two male and two female patients were selected between the ages of 25 and 47. None of the patients were taking prescription drugs at the time samples were isolated.

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Surgical specimens of diseased colon from patients with ulcerative colitis and Crohns disease and adjacent matched tissues were obtained from Clinomics. Bowel tissue from three female and three male Crohn's patients between the ages of 41-69 were used. Two patients were not on prescription medication while the others were taking dexamethasone, phenobarbital, or tylenol. Ulcerative colitis tissue was from three male and four female patients. Four of the patients were taking lebvid and two were on phenobarbital.

Total RNA from post mortem lung tissue from trauma victims with no disease or with emphysema, asthma or COPD was purchased from Clinomics. Emphysema patients ranged in age from 40-70 and all were smokers, this age range was chosen to focus on patients with cigarette-linked emphysema and to avoid those patients with alpha-1anti-trypsin deficiencies. Asthma patients ranged in age from 36-75, and excluded smokers to prevent those patients that could also have COPD. COPD patients ranged in age from 35-80 and included both smokers and non-smokers. Most patients were taking corticosteroids, and bronchodilators.

In the labels employed to identify tissues in the AI_comprehensive panel_v1.0 panel, the following abbreviations are used:

AI = Autoimmunity

Syn = Synovial

Normal = No apparent disease

Rep22 /Rep20 = individual patients

RA = Rheumatoid arthritis

Backus = From Backus Hospital

OA = Osteoarthritis

(SS) (BA) (MF) = Individual patients

Adj = Adjacent tissue

Match control = adjacent tissues

-M = Male

-F = Female

COPD = Chronic obstructive pulmonary disease

Panels 5D and 5I

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The plates for Panel 5D and 5I include two control wells and a variety of cDNAs isolated from human tissues and cell lines with an emphasis on metabolic diseases. Metabolic tissues were obtained from patients enrolled in the Gestational Diabetes study. Cells were obtained during different stages in the differentiation of adipocytes from human mesenchymal stem cells. Human pancreatic islets were also obtained.

In the Gestational Diabetes study subjects are young (18 - 40 years), otherwise healthy women with and without gestational diabetes undergoing routine (elective) Caesarean section. After delivery of the infant, when the surgical incisions were being repaired/closed, the obstetrician removed a small sample

Patient 2: Diabetic Hispanic, overweight, not on insulin

Patient 7-9: Nondiabetic Caucasian and obese (BMI>30)

Patient 10: Diabetic Hispanic, overweight, on insulin

Patient 11: Nondiabetic African American and overweight

Patient 12: Diabetic Hispanic on insulin

Adiocyte differentiation was induced in donor progenitor cells obtained from Osirus (a division of Clonetics/BioWhittaker) in triplicate, except for Donor 3U which had only two replicates. Scientists at Clonetics isolated, grew and differentiated human mesenchymal stem cells (HuMSCs) for CuraGen based on the published protocol found in Mark F. Pittenger, et al., Multilineage Potential of Adult Human Mesenchymal Stem Cells Science Apr 2 1999: 143-147. Clonetics provided Trizol lysates or frozen pellets suitable for mRNA isolation and ds cDNA production. A general description of each donor is as follows:

Donor 2 and 3 U: Mesenchymal Stem cells, Undifferentiated Adipose

Donor 2 and 3 AM: Adipose, AdiposeMidway Differentiated

Donor 2 and 3 AD: Adipose, Adipose Differentiated

Human cell lines were generally obtained from ATCC (American Type Culture Collection), NCI or the German tumor cell bank and fall into the following tissue groups: kidney proximal convoluted tubule, uterine smooth muscle cells, small intestine, liver HepG2 cancer cells, heart primary stromal cells, and adrenal cortical adenoma cells. These cells are

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all cultured under standard recommended conditions and RNA extracted using the standard procedures. All samples were processed at CuraGen to produce single stranded cDNA.

Panel 5I contains all samples previously described with the addition of pancreatic islets from a 58 year old female patient obtained from the Diabetes Research Institute at the University of Miami School of Medicine. Islet tissue was processed to total RNA at an outside source and delivered to CuraGen for addition to panel 5I.

In the labels employed to identify tissues in the 5D and 5I panels, the following abbreviations are used:

GO Adipose = Greater Omentum Adipose

SK = Skeletal Muscle

UT = Uterus

PL = Placenta

AD = Adipose Differentiated

AM = Adipose Midway Differentiated

U = Undifferentiated Stem Cells

Panel CNSD.01

The plates for Panel CNSD.01 include two control wells and 94 test samples comprised of cDNA isolated from postmortem human brain tissue obtained from the Harvard Brain Tissue Resource Center. Brains are removed from calvaria of donors between 4 and 24 hours after death, sectioned by neuroanatomists, and frozen at -80°C in liquid nitrogen vapor. All brains are sectioned and examined by neuropathologists to confirm diagnoses with clear associated neuropathology.

Disease diagnoses are taken from patient records. The panel contains two brains from each of the following diagnoses: Alzheimer's disease, Parkinson's disease, Huntington's disease, Progressive Supernuclear Palsy, Depression, and "Normal controls". Within each of these brains, the following regions are represented: cingulate gyrus, temporal pole, globus palladus, substantia nigra, Brodman Area 4 (primary motor strip), Brodman Area 7 (parietal cortex), Brodman Area 9 (prefrontal cortex), and Brodman area 17 (occipital cortex). Not all brain regions are represented in all cases; e.g., Huntington's disease is characterized in part by neurodegeneration in the globus palladus, thus this region is impossible to obtain from

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confirmed Huntington's cases. Likewise Parkinson's disease is characterized by degeneration of the substantia nigra making this region more difficult to obtain. Normal control brains were examined for neuropathology and found to be free of any pathology consistent with neurodegeneration.

5   In the labels employed to identify tissues in the CNS panel, the following abbreviations are used:

PSP = Progressive supranuclear palsy

Sub Nigra = Substantia nigra

Glob Palladus= Globus palladus

10   Temp Pole = Temporal pole

Cing Gyr = Cingulate gyrus

BA 4 = Brodman Area 4

Panel CNS_Neurodegeneration_V1.0

The plates for Panel CNS_Neurodegeneration_V1.0 include two control wells and 47

15   test samples comprised of cDNA isolated from postmortem human brain tissue obtained from the Harvard Brain Tissue Resource Center (McLean Hospital) and the Human Brain and Spinal Fluid Resource Center (VA Greater Los Angeles Healthcare System). Brains are removed from calvaria of donors between 4 and 24 hours after death, sectioned by neuroanatomists, and frozen at -80°C in liquid nitrogen vapor. All brains are sectioned and

20   examined by neuropathologists to confirm diagnoses with clear associated neuropathology.

Disease diagnoses are taken from patient records. The panel contains six brains from Alzheimer's disease (AD) patients, and eight brains from "Normal controls" who showed no evidence of dementia prior to death. The eight normal control brains are divided into two categories: Controls with no dementia and no Alzheimer's like pathology (Controls) and

25   controls with no dementia but evidence of severe Alzheimer's like pathology, (specifically senile plaque load rated as level 3 on a scale of 0-3; 0 = no evidence of plaques, 3 = severe AD senile plaque load). Within each of these brains, the following regions are represented: hippocampus, temporal cortex (Brodman Area 21), parietal cortex (Brodman area 7), and occipital cortex (Brodman area 17). These regions were chosen to encompass all levels of

30   neurodegeneration in AD. The hippocampus is a region of early and severe neuronal loss in

AD; the temporal cortex is known to show neurodegeneration in AD after the hippocampus; the parietal cortex shows moderate neuronal death in the late stages of the disease; the occipital cortex is spared in AD and therefore acts as a "control" region within AD patients. Not all brain regions are represented in all cases.

5   In the labels employed to identify tissues in the CNS_Neurodegeneration_V1.0 panel, the following abbreviations are used:

AD = Alzheimer's disease brain; patient was demented and showed AD-like pathology upon autopsy

Control = Control brains; patient not demented, showing no neuropathology

10   Control (Path) = Control brains; pateint not demented but showing sever AD-like pathology

SupTemporal Ctx = Superior Temporal Cortex

Inf Temporal Ctx = Inferior Temporal Cortex

A. GMAP000818_D/CG100318-01, GMAP000818_B, and GMAP000818_A_2:
15   GPCR

Expression of genes GMAP000818_D, GMAP000818_B, and GMAP000818_A_2 was assessed using the primer-probe sets Ag2219, Ag2356 and Ag2210, described in Tables AA, AB and AC. Results of the RTQ-PCR runs are shown in Tables AD, AE and AF. Please note that GMAP000818_A_2 was previously known as GMAP000818_A.

20   Table AA. Probe Name Ag2219

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tgtacttcttcctgtgcaagct-3'	22	172	201
Probe	TET-5'-ttttcccttctgtgagttccccta-3'-TAMRA	24	211	202
Reverse	5'-cctgaaagatagcacagcatct-3'	22	235	203

Table AB. Probe Name Ag2356

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggagggtctggagactattctg-3'	22	56	204
Probe	TET-5'-acatcttcacccttatggggaacctg-3'-TAMRA	26	100	205
Reverse	5'-agacaatagccagcaagatgag-3'	22	126	206

Table AC. Probe Name Ag2210

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tgtacttcttcctgtgcaagct-3'	22	172	207
Probe	TET-5'-ttttcccttctgtgagttccccta-3'-TAMRA	24	211	208
Reverse	5'-cctgaaagatagcacagcatct-3'	22	235	209

Table AD. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2219, Run 207928587	Rel. Exp.(%) Ag2219, Run 218648846	Rel. Exp.(%) Ag2356, Run 208702284	Tissue Name	Rel. Exp.(%) Ag2219, Run 207928587	Rel. Exp.(%) Ag2219, Run 218648846	Rel. Exp.(%) Ag2356, Run 208702284
AD 1 Hippo	15.9	0.0	12.2	Control (Path) 3 Temporal Ctx	8.0	0.0	0.0
AD 2 Hippo	43.5	42.6	41.2	Control (Path) 4 Temporal Ctx	31.9	11.6	56.3
AD 3 Hippo	0.0	0.0	0.0	AD 1 Occipital Ctx	0.0	31.4	6.9
AD 4 Hippo	0.0	0.0	0.0	AD 2 Occipital Ctx (Missing)	0.0	0.0	0.0
AD 5 Hippo	18.8	39.5	0.0	AD 3 Occipital Ctx	15.9	10.6	0.0
AD 6 Hippo	**100.0**	66.9	**100.0**	AD 4 Occipital Ctx	8.4	0.0	13.0
Control 2 Hippo	10.4	17.9	42.3	AD 5 Occipital Ctx	8.4	47.3	34.6
Control 4 Hippo	10.9	12.4	9.5	AD 5 Occipital Ctx	0.0	0.0	0.0
Control (Path) 3 Hippo	0.0	0.0	15.5	Control 1 Occipital Ctx	0.0	0.0	0.0
AD 1	26.8	0.0	21.6	Control 2	0.0	8.4	0.0

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Temporal Ctx				Occipital Ctx			
AD 2 Temporal Ctx	35.1	51.4	18.0	Control 3 Occipital Ctx	14.0	10.7	37.1
AD 3 Temporal Ctx	0.0	0.0	8.4	Control 4 Occipital Ctx	0.0	0.0	0.0
AD 4 Temporal Ctx	37.6	17.9	38.2	Control (Path) 1 Occipital Ctx	9.7	56.3	0.0
AD 5 Inf Temporal Ctx	54.0	0.0	52.5	Control (Path) 2 Occipital Ctx	0.0	0.0	12.9
AD 5 Sup Temporal Ctx	25.5	43.5	80.1	Control (Path) 3 Occipital Ctx	0.0	0.0	0.0
AD 6 Inf Temporal Ctx	52.5	**100.0**	26.8	Control (Path) 4 Occipital Ctx	0.0	10.1	0.0
AD 6 Sup Temporal Ctx	80.7	79.6	53.2	Control 1 Parietal Ctx	0.0	0.0	9.8
Control 1 Temporal Ctx	0.0	0.0	0.0	Control 2 Parietal Ctx	0.0	10.1	0.0
Control 2 Temporal Ctx	8.8	47.3	10.7	Control 3 Parietal Ctx	6.1	0.0	14.7
Control 3 Temporal Ctx	0.0	9.8	25.5	Control (Path) 1 Parietal Ctx	28.1	36.9	0.0
Control 3 Temporal Ctx	8.7	0.0	0.0	Control (Path) 2 Parietal Ctx	8.1	10.2	5.8
Control (Path) 1 Temporal Ctx	7.3	69.3	40.6	Control (Path) 3 Parietal Ctx	0.0	0.0	0.0

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Control (Path) 2 Temporal Ctx	4.7	30.1	30.8	Control (Path) 4 Parietal Ctx	28.3	21.2	0.0

Table AE. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag2219, Run 224781587	Tissue Name	Rel. Exp.(%) Ag2219, Run 224781587
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.8
Primary Th2 rest	0.0	Small airway epithelium none	0.4
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.4
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.4	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	1.2
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	7.8
2ry Th1/Th2/Tr1 anti-	0.2	CCD1106 (Keratinocytes)	0.0

CD95 CH11		none	
LAK cells rest	0.4	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.0	NCI-H292 none	0.5
LAK cells IL-2+IFN gamma	0.0	NCI-H292 IL-4	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-9	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-13	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 3 day	0.7	HPAEC none	0.0
Two Way MLR 5 day	0.0	HPAEC TNF alpha + IL-1 beta	0.4
Two Way MLR 7 day	0.0	Lung fibroblast none	0.0
PBMC rest	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.3
PBMC PWM	0.0	Lung fibroblast IL-4	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-13	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes PWM	0.0	Dermal fibroblast CCD1070 rest	0.0
B lymphocytes CD40L and IL-4	0.4	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.5
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast IFN gamma	1.3
Dendritic cells none	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells LPS	0.0	Dermal Fibroblasts rest	0.0
Dendritic cells anti-CD40	0.0	Neutrophils TNFa+LPS	0.4
Monocytes rest	0.0	Neutrophils rest	0.0
Monocytes LPS	0.0	Colon	1.1
Macrophages rest	0.0	Lung	4.8
Macrophages LPS	0.0	Thymus	7.7
HUVEC none	0.0	Kidney	**100.0**
HUVEC starved	0.7		

Table AF. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2210, Run 163624919	Rel. Exp.(%) Ag2219, Run 163724321	Rel. Exp.(%) Ag2356, Run 164038261	Tissue Name	Rel. Exp.(%) Ag2210, Run 163624919	Rel. Exp.(%) Ag2219, Run 163724321	Rel. Exp.(%) Ag2356, Run 164038261
Secondary Th1 act	0.0	0.0	0.0	HUVEC IL-1beta	0.0	0.0	0.0
Secondary Th2 act	0.0	0.0	0.0	HUVEC IFN gamma	0.0	0.0	5.5
Secondary Tr1 act	0.0	0.0	3.7	HUVEC TNF alpha + IFN gamma	0.0	0.0	0.0
Secondary Th1 rest	0.0	0.0	0.0	HUVEC TNF alpha + IL4	0.0	0.0	0.0
Secondary Th2 rest	4.5	0.0	0.0	HUVEC IL-11	4.3	0.0	0.0
Secondary Tr1 rest	4.7	0.0	0.0	Lung Microvascular EC none	0.0	0.0	10.2
Primary Th1 act	0.0	0.0	3.3	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0	0.0
Primary Th2 act	0.0	0.0	0.0	Microvascular Dermal EC none	0.0	0.0	0.0
Primary Tr1 act	0.0	0.0	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0	0.0
Primary Th1 rest	0.0	0.0	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0	14.3
Primary Th2 rest	0.0	0.0	2.1	Small airway epithelium none	7.9	9.4	6.5
Primary Tr1 rest	2.7	2.5	0.0	Small airway epithelium TNFalpha + IL-1beta	31.4	26.4	30.6
CD45RA CD4 lymphocyte act	0.0	0.0	0.0	Coronery artery SMC rest	0.0	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	3.5	0.0	0.0
CD8 lymphocyte	0.0	0.0	0.0	Astrocytes rest	3.3	0.0	0.0

act							
Secondary CD8 lymphocyte rest	0.0	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0	0.0
Secondary CD8 lymphocyte act	0.0	0.0	0.0	KU-812 (Basophil) rest	16.5	19.6	20.0
CD4 lymphocyte none	0.0	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	**100.0**	**100.0**	**100.0**
2ry Th1/Th2/Tr1_anti-CD95 CH11	4.6	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0	0.0
LAK cells rest	4.7	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0	3.6
LAK cells IL-2	0.0	0.0	0.0	Liver cirrhosis	8.5	36.3	22.5
LAK cells IL-2+IL-12	0.0	5.3	0.0	Lupus kidney	4.4	0.0	0.0
LAK cells IL-2+IFN gamma	0.0	0.0	0.0	NCI-H292 none	0.0	0.0	3.9
LAK cells IL-2+IL-18	3.9	0.0	2.0	NCI-H292 IL-4	0.0	0.0	0.0
LAK cells PMA/ionomycin	4.4	0.0	0.0	NCI-H292 IL-9	0.0	0.0	0.0
NK Cells IL-2 rest	0.0	0.0	0.0	NCI-H292 IL-13	0.0	0.0	0.0
Two Way MLR 3 day	0.0	0.0	0.0	NCI-H292 IFN gamma	0.0	0.0	5.6
Two Way MLR 5 day	0.0	4.8	0.0	HPAEC none	0.0	0.0	0.0
Two Way MLR 7 day	0.0	0.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	4.5	0.0
PBMC rest	0.0	0.0	0.0	Lung fibroblast none	4.3	0.0	4.3
PBMC PWM	0.0	4.3	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	7.5	0.0
PBMC PHA-L	0.0	0.0	0.0	Lung fibroblast IL-4	0.0	0.0	0.0
Ramos (B cell) none	0.0	0.0	4.2	Lung fibroblast IL-9	0.0	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	0.0	Lung fibroblast IL-13	0.0	0.0	0.0

B lymphocytes PWM	0.0	8.0	0.0	Lung fibroblast IFN gamma	0.0	0.0	0.0
B lymphocytes CD40L and IL-4	3.6	3.2	0.0	Dermal fibroblast CCD1070 rest	0.0	0.0	0.0
EOL-1 dbcAMP	0.0	6.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	0.0	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	3.4	12.8	Dermal fibroblast CCD1070 IL-1 beta	3.4	0.0	0.0
Dendritic cells none	0.0	4.3	0.0	Dermal fibroblast IFN gamma	0.0	0.0	0.0
Dendritic cells LPS	0.0	0.0	0.0	Dermal fibroblast IL-4	8.1	0.0	0.0
Dendritic cells anti-CD40	0.0	0.0	0.0	IBD Colitis 2	9.9	0.0	3.5
Monocytes rest	0.0	0.0	0.0	IBD Crohn's	5.2	0.0	0.0
Monocytes LPS	0.0	0.0	0.0	Colon	10.3	0.0	0.0
Macrophages rest	8.0	0.0	4.9	Lung	0.0	5.4	0.0
Macrophages LPS	0.0	0.0	0.0	Thymus	4.0	0.0	8.7
HUVEC none	0.0	4.2	0.0	Kidney	0.0	5.4	0.0
HUVEC starved	2.9	0.0	0.0				

CNS_neurodegeneration_v1.0 Summary: Ag2219 This gene is expressed at low but significant levels in the brain in one experiment with this probe/primer set and encodes a putative GPCR. Several neurotransmitter receptors are GPCRs, including the dopamine receptor family, the serotonin receptor family, the GABAB receptor, muscarinic acetylcholine receptors, and others; thus this GPCR may represent a novel neurotransmitter receptor. Targeting various neurotransmitter receptors (dopamine, serotonin) has proven to be an effective therapy in psychiatric illnesses such as schizophrenia, bipolar disorder, and depression. Furthermore, the cerebral cortex and hippocampus are regions of the brain that are known to be involved in Alzheimer's disease, seizure disorders, and in the normal process of memory formation. Therefore, therapeutic modulation of this gene or its protein product may be beneficial in the treatment of one or more of these diseases, as may stimulation and/or blockade of the receptor coded for by the gene. Ag2210 Expression of this gene is low/undetectable (CTs > 35) in all of the samples on this panel (data not shown).

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Panel 1.3D Summary: Ag2210/Ag2219/Ag2356 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag2210/Ag2219 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5   **Panel 2D Summary:** Ag2356 Expression of this gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

Panel 4.1D Summary: Ag2219 Expression of this gene is highest in the kidney (CT = 30.5). The putative GPCR encoded for by this gene could allow cells within the kidney to respond to specific microenvironmental signals (For example, ref. 1). Therefore, antibody or small

10   molecule therapies designed with the protein encoded for by this gene could modulate kidney function and be important in the treatment of inflammatory or autoimmune diseases that affect the kidney, including lupus and glomerulonephritis. This gene is also expressed at low but significant levels in the PMA and ionomycin treated basophil cell line KU-812 (CT = 34); this result is consistent with what is observed in Panel 4D. Low expression is also detected in

15   thymus and colon in this experiment.

References:

1. Mark M.D., Wittemann S., Herlitze S. (2000) G protein modulation of recombinant P/Q-type calcium channels by regulators of G protein signalling proteins. J. Physiol. 528 Pt 1: 65-77.

20   1. Fast synaptic transmission is triggered by the activation of presynaptic Ca2+ channels which can be inhibited by Gbetagamma subunits via G protein-coupled receptors (GPCR). Regulators of G protein signalling (RGS) proteins are GTPase-accelerating proteins (GAPs), which are responsible for >100-fold increases in the GTPase activity of G proteins and might be involved in the regulation of presynaptic Ca2+ channels. In this study we investigated the

25   effects of RGS2 on G protein modulation of recombinant P/Q-type channels expressed in a human embryonic kidney (HEK293) cell line using whole-cell recordings. 2. RGS2 markedly accelerates transmitter-mediated inhibition and recovery from inhibition of Ba2+ currents (IBa) through P/Q-type channels heterologously expressed with the muscarinic acetylcholine receptor M2 (mAChR M2). 3. Both RGS2 and RGS4 modulate the prepulse facilitation

30   properties of P/Q-type Ca2+ channels. G protein reinhibition is accelerated, while release

from inhibition is slowed. These kinetics depend on the availability of G protein alpha and betagamma subunits which is altered by RGS proteins. 4. RGS proteins unmask the Ca2+ channel beta subunit modulation of Ca2+ channel G protein inhibition. In the presence of RGS2, P/Q-type channels containing the beta2a and beta3 subunits reveal significantly altered kinetics of G protein modulation and increased facilitation compared to Ca2+ channels coexpressed with the beta1b or beta4 subunit.

PMID: 11018106

Panel 4D Summary: Ag2210/Ag2219/Ag2356 This transcript is expressed in the PMA and ionomycin treated basophil cell line KU-812 (CT = 33) and to a lesser extent in untreated KU-812 cells (CT = 35). This gene encodes a putative GPCR and it is known that GPCR-type receptors are important in multiple physiological responses mediated by basophils (ref. 1). Therefore, antibody or small molecule therapies designed with the protein encoded for by this gene could block or inhibit inflammation or tissue damage due to basophil activation in response to asthma, allergies, hypersensitivity reactions, psoriasis, and viral infections.

References:

1. Heinemann A., Hartnell A., Stubbs V.E., Murakami K., Soler D., LaRosa G., Askenase P.W., Williams T.J., Sabroe I. (2000) Basophil responses to chemokines are regulated by both sequential and cooperative receptor signaling. J. Immunol. 165: 7224-7233.

To investigate human basophil responses to chemokines, we have developed a sensitive assay that uses flow cytometry to measure leukocyte shape change as a marker of cell responsiveness. PBMC were isolated from the blood of volunteers. Basophils were identified as a single population of cells that stained positive for IL-3Ralpha (CDw123) and negative for HLA-DR, and their increase in forward scatter (as a result of cell shape change) in response to chemokines was measured. Shape change responses of basophils to chemokines were highly reproducible, with a rank order of potency: monocyte chemoattractant protein (MCP) 4 (peak at /= eotaxin-2 = eotaxin-3 >/= eotaxin > MCP-1 = MCP-3 > macrophage-inflammatory protein-1alpha > RANTES = MCP-2 = IL-8. The CCR4-selective ligand macrophage-derived chemokine did not elicit a response at concentrations up to 10 nM. Blocking mAbs to CCR2 and CCR3 demonstrated that responses to higher concentrations (>10 nM) of MCP-1 were mediated by CCR3 rather than CCR2, whereas MCP-4 exhibited a biphasic response consistent with sequential activation of CCR3 at lower concentrations and

CCR2 at 10 nM MCP-4 and above. In contrast, responses to MCP-3 were blocked only in the presence of both mAbs, but not after pretreatment with either anti-CCR2 or anti-CCR3 mAb alone. These patterns of receptor usage were different from those seen for eosinophils and monocytes. We suggest that cooperation between CCRs might be a mechanism for preferential recruitment of basophils, as occurs in tissue hypersensitivity responses in vivo.

PMID: 11120855

B. GMAC011647_D/ CG55970-04: GPCR

Expression of gene GMAC011647_D was assessed using the primer-probe sets Ag5095 and Ag2215, described in Tables BA and BB. Results of the RTQ-PCR runs are shown in Tables BC, BD, BE, BF and BG.

Table BA. Probe Name Ag5095

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ttctgctgctgctttatgct-3'	20	103	210
Probe	TET-5'-cctgggcaacatcctcatcctcttta-3'-TAMRA	26	131	211
Reverse	5'-gcaagctctgctcttccttt-3'	20	161	212

Table BB. Probe Name Ag2215

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tgtctctttgtacctccaatgc-3'	22	844	213
Probe	TET-5'-cccaattatctattccatcaagactaagga-3'-TAMRA	30	870	214
Reverse	5'-cttgtgtagtctcctgcgaatc-3'	22	900	215

Table BC. General_screening_panel_v1.5

Tissue Name	Rel. Exp.(%) Ag5095, Run 228727262	Rel. Exp.(%) Ag5095, Run 229384819	Tissue Name	Rel. Exp.(%) Ag5095, Run 228727262	Rel. Exp.(%) Ag5095, Run 229384819
Adipose	0.1	0.1	Renal ca. TK-10	0.1	0.0
Melanoma* Hs688(A).T	0.0	0.0	Bladder	0.4	0.4
Melanoma*	0.0	0.0	Gastric ca. (liver	0.2	0.2

Hs688(B).T			met.) NCI-N87		
Melanoma* M14	0.2	0.1	Gastric ca. KATO III	0.2	0.3
Melanoma* LOXIMVI	2.0	1.5	Colon ca. SW-948	0.0	0.0
Melanoma* SK-MEL-5	23.3	24.3	Colon ca. SW480	0.2	0.2
Squamous cell carcinoma SCC-4	0.0	0.0	Colon ca.* (SW480 met) SW620	1.6	1.1
Testis Pool	0.2	0.2	Colon ca. HT29	0.0	0.0
Prostate ca.* (bone met) PC-3	0.0	0.0	Colon ca. HCT-116	**100.0**	**100.0**
Prostate Pool	0.1	0.2	Colon ca. CaCo-2	0.1	0.0
Placenta	0.0	0.1	Colon cancer tissue	0.0	0.1
Uterus Pool	0.2	0.1	Colon ca. SW1116	0.0	0.0
Ovarian ca. OVCAR-3	0.1	0.1	Colon ca. Colo-205	0.0	0.0
Ovarian ca. SK-OV-3	0.5	0.7	Colon ca. SW-48	0.0	0.0
Ovarian ca. OVCAR-4	0.0	0.0	Colon Pool	0.7	0.5
Ovarian ca. OVCAR-5	0.0	0.0	Small Intestine Pool	0.6	1.1
Ovarian ca. IGROV-1	0.0	0.0	Stomach Pool	0.3	0.3
Ovarian ca. OVCAR-8	0.0	0.0	Bone Marrow Pool	0.3	0.2
Ovary	0.2	0.3	Fetal Heart	0.3	0.3
Breast ca. MCF-7	0.0	0.0	Heart Pool	0.2	0.1
Breast ca. MDA-MB-231	0.0	0.0	Lymph Node Pool	0.5	0.6
Breast ca. BT 549	0.0	0.0	Fetal Skeletal Muscle	0.1	0.1
Breast ca. T47D	0.0	0.0	Skeletal Muscle Pool	0.1	0.0
Breast ca.	2.2	3.0	Spleen Pool	0.1	0.1

MDA-N					
Breast Pool	0.6	0.4	Thymus Pool	0.3	0.4
Trachea	0.1	0.2	CNS cancer (glio/astro) U87-MG	0.0	0.0
Lung	0.3	0.2	CNS cancer (glio/astro) U-118-MG	0.2	0.2
Fetal Lung	0.4	0.7	CNS cancer (neuro;met) SK-N-AS	0.0	0.0
Lung ca. NCI-N417	0.0	0.0	CNS cancer (astro) SF-539	0.0	0.0
Lung ca. LX-1	16.7	19.5	CNS cancer (astro) SNB-75	0.0	0.0
Lung ca. NCI-H146	0.1	0.0	CNS cancer (glio) SNB-19	0.0	0.0
Lung ca. SHP-77	0.3	0.1	CNS cancer (glio) SF-295	0.3	0.2
Lung ca. A549	0.1	0.0	Brain (Amygdala) Pool	0.0	0.0
Lung ca. NCI-H526	0.0	0.0	Brain (cerebellum)	0.0	0.0
Lung ca. NCI-H23	0.0	0.0	Brain (fetal)	0.1	0.1
Lung ca. NCI-H460	0.9	0.0	Brain (Hippocampus) Pool	0.0	0.0
Lung ca. HOP-62	0.0	0.0	Cerebral Cortex Pool	0.0	0.0
Lung ca. NCI-H522	0.0	0.0	Brain (Substantia nigra) Pool	0.0	0.0
Liver	0.0	0.0	Brain (Thalamus) Pool	0.1	0.1
Fetal Liver	0.0	0.1	Brain (whole)	0.1	0.1
Liver ca. HepG2	0.0	0.0	Spinal Cord Pool	0.0	0.1
Kidney Pool	0.4	0.9	Adrenal Gland	0.1	0.1
Fetal Kidney	0.7	0.5	Pituitary gland Pool	0.0	0.1
Renal ca. 786-0	0.0	0.0	Salivary Gland	0.0	0.0
Renal ca. A498	0.0	0.0	Thyroid (female)	0.0	0.0

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Renal ca. ACHN	0.0	0.1	Pancreatic ca. CAPAN2	0.0	0.0
Renal ca. UO-31	0.0	0.0	Pancreas Pool	0.5	0.6

Table BD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2215, Run 165974923	Tissue Name	Rel. Exp.(%) Ag2215, Run 165974923
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.5	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.6
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	1.5	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	1.8	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.4
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	38.4
Brain (thalamus)	0.5	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	1.2
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
Glio/astro U87-MG	0.6	Lung ca. (non-sm. cell) A549	0.0
Glio/astro U-118-MG	0.6	Lung ca. (non-s.cell) NCI-H23	1.3
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	0.4	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.7	Lung ca. (squam.) SW 900	0.5
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0

glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.5	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.5	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	3.8
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.6
Thymus	0.6	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.6	Ovarian ca. OVCAR-8	0.0
Colorectal	1.1	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	4.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.5
Colon ca.* SW620 (SW480 met)	2.5	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	0.0
Colon ca. HCT-116	**100.0**	Testis	0.9
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.5
Bladder	1.7	Melanoma LOX IMVI	7.7
Trachea	0.6	Melanoma* (met) SK-MEL-5	40.9
Kidney	0.0	Adipose	0.0

Table BE. Panel 2.2

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Tissue Name	Rel. Exp.(%) Ag2215, Run 174285449	Tissue Name	Rel. Exp.(%) Ag2215, Run 174285449
Normal Colon	0.4	Kidney Margin (OD04348)	6.3
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.3
Colon Margin (OD06064)	0.4	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.3	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.2	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.5	Kidney Cancer 9010320	0.8
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.9
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	1.4
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	17.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	1.9
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	6.1
Normal Prostate	0.3	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.7	Thyroid Cancer	0.0
Prostate Margin (OD04410)	0.4	Thyroid Cancer A302152	0.5
Normal Ovary	0.0	Thyroid Margin A302153	1.1
Ovarian cancer (OD06283-03)	0.0	Normal Breast	3.1
Ovarian Margin (OD06283-07)	1.3	Breast Cancer	**100.0**
Ovarian Cancer	0.0	Breast Cancer	0.0
Ovarian cancer (OD06145)	1.4	Breast Cancer (OD04590-01)	0.0
Ovarian Margin	0.6	Breast Cancer Mets	0.0

(OD06145)		(OD04590-03)	
Ovarian cancer (OD06455-03)	0.6	Breast Cancer Metastasis	0.5
Ovarian Margin (OD06455-07)	1.3	Breast Cancer	0.6
Normal Lung	0.4	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	2.2	Breast Margin 9100265	0.4
Lung Margin (ODO4945-03)	0.6	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.4	Breast cancer (OD06083)	1.6
Lung Cancer (OD05014A)	0.4	Breast cancer node metastasis (OD06083)	0.5
Lung Margin (OD05014B)	0.2	Normal Liver	0.8
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.2
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.4
Lung Margin (OD04237-02)	0.9	Liver Tissue 6004-N	0.4
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0
Liver Margin (ODO4310)	0.4	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer	0.3
Lung Margin (OD04321)	0.0	Normal Bladder	0.7
Normal Kidney	0.9	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	2.9	Bladder Cancer	0.0
Kidney Margin (OD04338)	0.5	Normal Stomach	1.6
Kidney Ca Nuclear grade 1/2 (OD04339)	1.7	Gastric Cancer 9060397	1.4
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	2.5
Kidney Margin	0.5	Stomach Margin	0.0

(OD04340)		9060394	
Kidney Ca, Nuclear grade 3 (OD04348)	0.4	Gastric Cancer 064005	0.0

Table BF. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag5095, Run 225001774	Tissue Name	Rel. Exp.(%) Ag5095, Run 225001774
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.9
Secondary Tr1 act	0.2	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.6
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.3	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.7	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.5	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.8	Coronery artery SMC TNFalpha + IL-1beta	0.4
CD8 lymphocyte act	0.0	Astrocytes rest	0.8
Secondary CD8 lymphocyte rest	0.2	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.8
2ry Th1/Th2/Tr1_anti-CD95 CH11	1.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0

LAK cells IL-2	1.2	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.6	NCI-H292 none	0.4
LAK cells IL-2+IFN gamma	0.0	NCI-H292 IL-4	0.0
LAK cells IL-2+ IL-18	0.2	NCI-H292 IL-9	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-13	0.0
NK Cells IL-2 rest	0.6	NCI-H292 IFN gamma	0.0
Two Way MLR 3 day	1.8	HPAEC none	0.0
Two Way MLR 5 day	1.1	HPAEC TNF alpha + IL-1 beta	0.0
Two Way MLR 7 day	0.0	Lung fibroblast none	0.0
PBMC rest	0.8	Lung fibroblast TNF alpha + IL-1 beta	0.8
PBMC PWM	0.0	Lung fibroblast IL-4	0.4
PBMC PHA-L	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) none	17.0	Lung fibroblast IL-13	1.2
Ramos (B cell) ionomycin	13.2	Lung fibroblast IFN gamma	0.4
B lymphocytes PWM	0.3	Dermal fibroblast CCD1070 rest	0.0
B lymphocytes CD40L and IL-4	0.7	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast IFN gamma	1.4
Dendritic cells none	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells LPS	0.3	Dermal Fibroblasts rest	0.0
Dendritic cells anti-CD40	0.0	Neutrophils TNFa+LPS	0.0
Monocytes rest	0.0	Neutrophils rest	2.0
Monocytes LPS	0.8	Colon	1.6
Macrophages rest	1.4	Lung	4.6
Macrophages LPS	0.0	Thymus	9.4
HUVEC none	0.2	Kidney	**100.0**
HUVEC starved	0.4		

Table BG. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2215, Run 163633530	Tissue Name	Rel. Exp.(%) Ag2215, Run 163633530

Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	1.4	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.6
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	1.7	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.9	Small airway epithelium none	0.0
Primary Tr1 rest	0.4	Small airway epithelium TNFalpha + IL-1beta	1.3
CD45RA CD4 lymphocyte act	0.4	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	2.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	2.4	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	3.1	Liver cirrhosis	3.1
LAK cells IL-2+IL-12	0.0	Lupus kidney	1.3
LAK cells IL-2+IFN gamma	1.7	NCI-H292 none	1.7
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	1.6
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.6

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Two Way MLR 3 day	2.7	NCI-H292 IFN gamma	1.1
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	1.4	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.7	Lung fibroblast none	1.0
PBMC PWM	0.6	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	30.6	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	**100.0**	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.5	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	1.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.6
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.7	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	1.3
Dendritic cells anti-CD40	0.0	IBD Colitis 2	2.5
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.8
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	19.6
HUVEC none	0.0	Kidney	10.7
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: <u>Ag5095</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.5 Summary: <u>Ag5095</u> Results from two experiments using the same probe/primer set are in good agreement. The expression of this gene appears to be highest in a samples derived from a colon cancer cell line (HCT 116). In addition there appears to be expression in a lung cancer cell line (LX-1) and a melanoma cell line (SK-Mel-5). Thus, the expression of this gene could be used to distinguish samples derived from these cell lines when compared to the other samples in the panel. Moreover, therapeutic modulation

of this gene product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of colon cancer, lung cancer or melanoma.

Among tissues with metabolic activity, this gene is expressed at low levels in pancreas and fetal heart. Therefore, the GPCR encoded by this gene may play a role in cardiovascular diseases and/or metabolic diseases, such as diabetes and obesity. Low expression is also seen in a number of other normal tissues including thymus, lymph node, bone marrow, small intestine, stomach, colon, bladder, lung, breast, and ovary (CTs = 31-35).

Panel 1.3D Summary: Ag2215 Low but significant expression of this gene is seen in a colon cancer cell line, a lung cancer cell line and two melanoma cell lines. Thus, the expression of this gene could be used to distinguish samples derived from these cell lines when compared to the other samples in the panel. Moreover, therapeutic modulation of this gene product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of colon cancer, lung cancer or melanoma. These results are consistent with what is observed in General_screening_panel_v1.5.

Panel 2.2 Summary: Ag2215 The expression of this gene appears to be highest in a sample derived from a breast cancer specimen (CT = 30). Thus, the expression of this gene could be used to distinguish this malignant breast specimen from the other samples in the panel. In addition, there is low but substantial expression in two samples of normal kidney tissue adjacent to malignant kidney tissue. This latter observation is of note as there is no expression in the malignant kidney tissue itself. Moreover, therapeutic modulation of this gene product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of breast cancer or kidney cancer.

Panel 4.1D Summary: Ag5095 Expression of this gene is highest in kidney (CT = 30). Therefore, the putative GPCR encoded for by this gene could allow cells within the kidney to respond to specific microenvironmental signals. Thus, antibody or small molecule therapies designed with the protein encoded for by this gene could modulate kidney function and be important in the treatment of inflammatory or autoimmune diseases that affect the kidney, including lupus and glomerulonephritis.

In addition, this gene is expressed at low levels in Ramos B cells (CT = 33), consistent with what is observed in Panel 4D. Expression of this transcript in B cells

suggests that this gene may be involved in rheumatic disease including rheumatoid arthritis, lupus, osteoarthritis, and hyperproliferative B cell disorders.

Panel 4D Summary: Ag2215 Expression of this gene is highest in Ramos B cells treated with ionomycin (CT = 31). Therefore, expression of this gene could be used to distinguish B cells from the other samples on this panel. In addition, expression of this transcript in B cells suggests that this gene may be involved in rheumatic diseases including rheumatoid arthritis, lupus, osteoarthritis, and hyperproliferative B cell disorders.

C. GMAC011654_A/CG143977-01: GPCR

Expression of gene GMAC011654_A (also known as CG143977-01) was assessed using the primer-probe set Ag2206, described in Table CA. Results of the RTQ-PCR runs are shown in Tables CB, CC, and CD.

Table CA. Probe Name Ag2206

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ctttctgaaatctggccagttt-3'	22	463	216
Probe	TET-5'-tgccacttttcagcttactttctgca-3'-TAMRA	26	486	217
Reverse	5'-caattgtcctcggtcacaataa-3'	22	534	218

Table CB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2206, Run 166003995	Tissue Name	Rel. Exp.(%) Ag2206, Run 166003995
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	75.8	Renal ca. UO-31	0.0
Pituitary gland	26.4	Renal ca. TK-10	26.8
Brain (fetal)	97.9	Liver	0.0
Brain (whole)	43.8	Liver (fetal)	0.0
Brain (amygdala)	62.9	Liver ca.	13.4

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		(hepatoblast) HepG2	
Brain (cerebellum)	18.8	Lung	0.0
Brain (hippocampus)	18.3	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	8.8
Brain (thalamus)	14.7	Lung ca. (small cell) NCI-H69	12.2
Cerebral Cortex	17.2	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	43.2	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	25.7	Lung ca. (non-s.cell) NCI-H23	**100.0**
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	28.1	Mammary gland	21.2
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	32.8
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	16.8
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	4.9
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	15.4

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Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	20.3
Colon ca. SW480	12.4	Placenta	0.0
Colon ca.* SW620 (SW480 met)	15.8	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	0.0
Colon ca. HCT-116	0.0	Testis	31.9
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	3.7	Melanoma LOX IMVI	8.2
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	38.2	Adipose	0.0

Table CC. Panel 2D

Tissue Name	Rel. Exp.(%) Ag2206, Run 164025884	Tissue Name	Rel. Exp.(%) Ag2206, Run 164025884
Normal Colon	6.2	Kidney Margin 8120608	3.6
CC Well to Mod Diff (ODO3866)	0.0	Kidney Cancer 8120613	0.0
CC Margin (ODO3866)	6.9	Kidney Margin 8120614	10.5
CC Gr.2 rectosigmoid (ODO3868)	5.1	Kidney Cancer 9010320	1.9
CC Margin (ODO3868)	0.0	Kidney Margin 9010321	18.9
CC Mod Diff (ODO3920)	1.8	Normal Uterus	2.0
CC Margin (ODO3920)	6.7	Uterine Cancer 064011	31.4
CC Gr.2 ascend colon (ODO3921)	8.3	Normal Thyroid	9.8
CC Margin (ODO3921)	6.1	Thyroid Cancer	7.0

CC from Partial Hepatectomy (ODO4309) Mets	6.4	Thyroid Cancer A302152	0.0
Liver Margin (ODO4309)	4.0	Thyroid Margin A302153	19.6
Colon mets to lung (OD04451-01)	7.2	Normal Breast	29.7
Lung Margin (OD04451-02)	0.0	Breast Cancer	3.7
Normal Prostate 6546-1	24.8	Breast Cancer (OD04590-01)	2.6
Prostate Cancer (OD04410)	1.8	Breast Cancer Mets (OD04590-03)	11.9
Prostate Margin (OD04410)	5.0	Breast Cancer Metastasis	**100.0**
Prostate Cancer (OD04720-01)	49.0	Breast Cancer	20.6
Prostate Margin (OD04720-02)	11.4	Breast Cancer	57.4
Normal Lung	14.3	Breast Cancer 9100266	2.6
Lung Met to Muscle (ODO4286)	0.0	Breast Margin 9100265	0.0
Muscle Margin (ODO4286)	2.2	Breast Cancer A209073	6.2
Lung Malignant Cancer (OD03126)	2.3	Breast Margin A2090734	6.8
Lung Margin (OD03126)	9.2	Normal Liver	10.9
Lung Cancer (OD04404)	0.0	Liver Cancer	2.0
Lung Margin (OD04404)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04565)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD04565)	3.8	Liver Cancer 6004-T	1.6
Lung Cancer (OD04237-01)	25.5	Liver Tissue 6004-N	4.0
Lung Margin (OD04237-02)	5.8	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	0.0	Normal Bladder	22.4
Melanoma Metastasis	6.4	Bladder Cancer	6.1
Lung Margin (OD04321)	0.0	Bladder Cancer	7.5
Normal Kidney	50.0	Bladder Cancer (OD04718-01)	0.0

Kidney Ca, Nuclear grade 2 (OD04338)	51.1	Bladder Normal Adjacent (OD04718-03)	11.7
Kidney Margin (OD04338)	15.8	Normal Ovary	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Ovarian Cancer	13.5
Kidney Margin (OD04339)	30.4	Ovarian Cancer (OD04768-07)	1.7
Kidney Ca, Clear cell type (OD04340)	23.8	Ovary Margin (OD04768-08)	0.0
Kidney Margin (OD04340)	17.7	Normal Stomach	2.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 9060358	1.8
Kidney Margin (OD04348)	30.1	Stomach Margin 9060359	1.8
Kidney Cancer (OD04622-01)	2.1	Gastric Cancer 9060395	0.8
Kidney Margin (OD04622-03)	3.0	Stomach Margin 9060394	0.0
Kidney Cancer (OD04450-01)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04450-03)	9.9	Stomach Margin 9060396	0.0
Kidney Cancer 8120607	2.1	Gastric Cancer 064005	12.2

Table CD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2206, Run 161905859	Tissue Name	Rel. Exp.(%) Ag2206, Run 161905859
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	1.1	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	1.3
Secondary Tr1 rest	0.0	Lung Microvascular EC none	4.6
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC	0.0

		none	
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	2.4	Bronchial epithelium TNFalpha + IL1beta	21.6
Primary Th2 rest	0.9	Small airway epithelium none	5.5
Primary Tr1 rest	1.5	Small airway epithelium TNFalpha + IL-1beta	19.3
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	4.7
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	7.7
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	15.7
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	33.4
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	4.2
LAK cells rest	1.1	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	7.5
LAK cells IL-2+IL-12	1.1	Lupus kidney	1.1
LAK cells IL-2+IFN gamma	0.5	NCI-H292 none	7.4
LAK cells IL-2+ IL-18	1.0	NCI-H292 IL-4	7.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	4.8
NK Cells IL-2 rest	1.3	NCI-H292 IL-13	2.9
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	2.7
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	1.6
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	1.1	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.7	Lung fibroblast IL-9	0.9
Ramos (B cell) ionomycin	3.8	Lung fibroblast IL-13	0.0

B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	97.9	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	**100.0**	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	3.4	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	1.4	IBD Colitis 2	0.4
Monocytes rest	1.0	IBD Crohn's	0.8
Monocytes LPS	2.3	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	20.2
HUVEC none	1.0	Kidney	2.9
HUVEC starved	3.4		

CNS_neurodegeneration_v1.0 Summary: <u>Ag2206</u> Data from one experiment using this probe/primer set was not included because the amp plot indicates that there was a problem with one of the wells (data not shown).

Panel 1.3D Summary: <u>Ag2206</u> Expression of the GMAC011654_A gene is highest in a sample derived from a lung cancer cell line (NCI-H23) (CT = 34.4). In addition, there is low but substantial expression of this gene in samples derived from fetal brain and salivary gland. Apparent expression seen in other samples is below the threshold for reliable evaluation. Thus, the expression of this gene could be used to distinguish samples derived from fetal brain, salivary gland and NCI-H23 cells when compared to the other samples in the panel. Moreover, therapeutic modulation of this gene product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of lung cancer or diseases of the central nervous system.

Panel 2D Summary: <u>Ag2206</u> Expression of the GMAC011654_A gene is highest in a sample derived from a breast cancer metastasis (CT = 32.3). Thus, the expression of this gene could be used to distinguish the breast cancer metastasis sample from the other samples in the panel. In addition, there is substantial expression in two more samples derived from breast

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cancer, as well as in normal breast tissue, a uterine cancer and a prostate cancer. Of note is the observation that in 5 of 9 instances there was substantial expression of this gene in the normal kidney tissue adjacent to malignant kidney. Therefore, the expression of this gene could also be used to distinguish between normal and malignant kidney. Moreover, therapeutic modulation of this gene product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of breast cancer, uterine cancer, prostate cancer or kidney cancer.

Panel 4D Summary: Ag2206 Expression of the GMAC011654_A gene is detected at the highest levels in resting and activated EOL-1 eosinophil cells (CT = 31). Lower levels of expression are also found in TNFalpha + IL-1beta stimulated small airway epithelium, TNFalpha + IL-1beta stimulated bronchial epithelium, KU-812 basophil cells stimulated with PMA/ionomycin and normal thymus. Owing to the importance of eosinophils and basophils in lung pathology and to the detection of this transcript in lung epithelial tissues, antibody or small molecule therapies designed with the protein encoded for by this gene could block or inhibit inflammation or tissue damage due to lung conditions including asthma, allergies, hypersensitivity reactions, and viral infections.

Panel CNS_1 Summary: Ag2206 Expression of this gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

D. GMAC004977_A/CG50193-02, GMAC011904_A, and SC120295344_A: GPCR

Expression of gene GMAC004977_A (also known as CG50193-02) and variants GMAC011904_A and SC120295344_A was assessed using the primer-probe sets Ag2201, Ag2433, Ag2479 and Ag2537, described in Tables DA, DB, DC and DD. Results of the RTQ-PCR runs are shown in Tables DE, DF, DG, DH and DI.

Table DA. Probe Name Ag2201

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggcagaagaatcagacctctct-3'	22	96	219
Probe	TET-5'-acttcatccttgaggggctcttcgat-3'-TAMRA	26	123	220

Reverse	5'-gagaaaaggaaaaggtgggtaa-3'	22	156	221

Table DB. Probe Name Ag2433

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ctcatctgggagcaagagaa-3'	20	775	222
Probe	TET-5'-acttgtggctcccacctcacggt-3'-TAMRA	23	806	223
Reverse	5'-aggcaccaaaccaaagaga-3'	19	833	224

Table DC. Probe Name Ag2479

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gaggagaatgctgctgatgtac-3'	22	688	225
Probe	TET-5'-tggtctcatacacagtgatgtcgcca-3'-TAMRA	26	658	226
Reverse	5'-ccagctgttgtgaagttggtat-3'	22	635	227

Table DD. Probe Name Ag2537

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gaggagaatgctgctgatgtac-3'	22	688	228
Probe	TET-5'-tggtctcatacacagtgatgtcgcca-3'-TAMRA	26	658	229
Reverse	5'-ccagctgttgtgaagttggtat-3'	22	635	230

5   Table DE. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2201, Run 207927803	Rel. Exp.(%) Ag2433, Run 228396997	Rel. Exp.(%) Ag2479, Run 208776912	Rel. Exp.(%) Ag2537, Run 208124100
AD 1 Hippo	0.0	5.4	1.8	1.6
AD 2 Hippo	8.2	5.9	8.0	4.0
AD 3 Hippo	4.1	1.6	3.3	6.3
AD 4 Hippo	2.6	0.0	4.5	6.1
AD 5 Hippo	16.5	23.0	22.4	21.8
AD 6 Hippo	46.7	31.2	58.2	25.9
Control 2 Hippo	2.3	2.1	1.5	4.3
Control 4	17.0	12.2	5.9	7.1

Hippo				
Control (Path) 3 Hippo	2.0	0.0	1.7	6.4
AD 1 Temporal Ctx	2.5	5.0	3.6	4.5
AD 2 Temporal Ctx	2.9	6.6	5.1	2.2
AD 3 Temporal Ctx	2.2	2.0	3.3	6.6
AD 4 Temporal Ctx	18.0	9.1	18.0	17.0
AD 5 Inf Temporal Ctx	15.6	22.7	29.3	14.0
AD 5 Sup Temporal Ctx	17.4	4.1	12.8	2.2
AD 6 Inf Temporal Ctx	40.9	93.3	69.7	62.4
AD 6 Sup Temporal Ctx	**100.0**	**100.0**	**100.0**	**100.0**
Control 1 Temporal Ctx	2.1	5.5	0.0	0.0
Control 2 Temporal Ctx	2.3	8.8	7.1	10.8
Control 3 Temporal Ctx	3.4	12.0	10.5	5.4
Control 3 Temporal Ctx	10.9	11.8	7.5	6.9
Control (Path) 1 Temporal Ctx	14.7	11.5	14.6	8.5
Control (Path) 2 Temporal Ctx	15.3	10.7	12.9	5.5
Control (Path) 3 Temporal Ctx	5.0	0.0	0.0	0.0
Control (Path) 4 Temporal Ctx	13.9	28.3	18.6	18.4
AD 1 Occipital Ctx	2.7	4.4	5.0	0.0
AD 2 Occipital Ctx (Missing)	0.0	0.0	0.0	0.0
AD 3 Occipital	13.6	6.0	2.0	4.8

Ctx				
AD 4 Occipital Ctx	12.8	7.4	19.2	17.1
AD 5 Occipital Ctx	21.9	10.7	22.4	11.7
AD 5 Occipital Ctx	6.1	2.5	2.1	3.6
Control 1 Occipital Ctx	0.0	2.5	3.5	0.4
Control 2 Occipital Ctx	1.9	7.0	12.6	2.1
Control 3 Occipital Ctx	2.0	12.8	7.7	4.0
Control 4 Occipital Ctx	9.1	3.9	6.3	8.9
Control (Path) 1 Occipital Ctx	9.4	11.3	15.0	14.6
Control (Path) 2 Occipital Ctx	18.3	7.3	15.0	9.9
Control (Path) 3 Occipital Ctx	0.0	6.3	1.8	0.0
Control (Path) 4 Occipital Ctx	18.9	11.3	15.9	7.6
Control 1 Parietal Ctx	0.0	5.8	1.8	1.3
Control 2 Parietal Ctx	15.9	14.1	8.4	10.6
Control 3 Parietal Ctx	5.5	10.2	8.5	3.5
Control (Path) 1 Parietal Ctx	5.5	14.4	11.1	5.6
Control (Path) 2 Parietal Ctx	5.6	6.1	8.6	12.4
Control (Path) 3 Parietal Ctx	1.7	0.0	2.8	1.5
Control (Path) 4 Parietal Ctx	20.6	19.9	25.3	15.4

Table DF. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2201, Run 165982030	Rel. Exp.(%) Ag2479, Run 165639425	Rel. Exp.(%) Ag2537, Run 165532774
Liver adenocarcinoma	8.2	11.9	6.5

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Pancreas	0.0	31.2	10.1
Pancreatic ca. CAPAN 2	0.0	0.0	0.0
Adrenal gland	8.7	7.2	11.6
Thyroid	0.0	5.4	2.3
Salivary gland	0.0	5.9	11.6
Pituitary gland	17.0	62.4	7.0
Brain (fetal)	8.4	0.0	11.3
Brain (whole)	4.7	40.9	0.0
Brain (amygdala)	16.2	46.3	12.6
Brain (cerebellum)	56.3	38.7	50.7
Brain (hippocampus)	5.6	31.6	25.7
Brain (substantia nigra)	0.0	21.8	10.8
Brain (thalamus)	23.8	13.2	0.0
Cerebral Cortex	3.2	12.3	9.4
Spinal cord	0.0	21.2	0.0
Glio/astro U87-MG	35.4	24.8	29.1
Glio/astro U-118-MG	17.6	18.8	20.2
astrocytoma SW1783	0.0	37.9	0.0
Neuro*; met SK-N-AS	8.9	9.8	7.5
astrocytoma SF-539	**100.0**	71.7	0.0
astrocytoma SNB-75	0.0	18.0	12.0
glioma SNB-19	9.0	8.7	8.6
glioma U251	18.2	36.9	90.8
glioma SF-295	45.1	83.5	**100.0**
Heart (Fetal)	12.2	10.0	0.0
Heart	0.0	0.0	0.0
Skeletal muscle (Fetal)	8.9	0.0	0.0
Skeletal muscle	0.0	0.0	0.0
Bone marrow	0.0	0.0	0.0
Thymus	22.1	0.0	11.3
Spleen	0.0	**100.0**	11.8
Lymph node	12.7	0.0	23.0
Colorectal	38.7	20.6	46.7
Stomach	0.0	0.0	37.6
Small intestine	9.7	21.0	23.7
Colon ca. SW480	0.0	0.0	0.0
Colon ca.* SW620 (SW480 met)	8.9	10.4	0.0
Colon ca. HT29	0.0	0.0	0.0

Colon ca. HCT-116	0.0	17.2	8.0
Colon ca. CaCo-2	0.0	23.0	11.6
CC Well to Mod Diff (ODO3866)	6.2	0.0	12.4
Colon ca. HCC-2998	7.7	13.1	0.0
Gastric ca. (liver met) NCI-N87	0.0	13.9	0.0
Bladder	21.8	5.0	0.0
Trachea	0.0	13.1	0.0
Kidney	0.0	11.9	0.0
Kidney (fetal)	9.4	24.5	0.0
Renal ca. 786-0	8.5	22.4	10.9
Renal ca. A498	23.7	44.4	9.3
Renal ca. RXF 393	0.0	22.5	0.0
Renal ca. ACHN	8.7	16.6	11.0
Renal ca. UO-31	0.0	0.0	0.0
Renal ca. TK-10	16.5	12.2	0.0
Liver	5.3	0.0	0.0
Liver (fetal)	0.0	0.0	0.0
Liver ca. (hepatoblast) HepG2	0.0	1.6	0.0
Lung	9.7	0.0	0.0
Lung (fetal)	7.7	0.0	14.4
Lung ca. (small cell) LX-1	8.7	36.6	26.2
Lung ca. (small cell) NCI-H69	0.0	11.0	0.0
Lung ca. (s.cell var.) SHP-77	9.2	11.3	0.0
Lung ca. (large cell)NCI-H460	0.0	18.2	0.0
Lung ca. (non-sm. cell) A549	0.0	9.5	0.0
Lung ca. (non-s.cell) NCI-H23	2.6	23.8	24.0
Lung ca. (non-s.cell) HOP-62	7.9	37.4	48.6
Lung ca. (non-s.cl) NCI-H522	6.1	0.0	9.1
Lung ca. (squam.) SW 900	10.3	0.0	12.3
Lung ca. (squam.)	15.4	0.0	12.4

NCI-H596			
Mammary gland	0.0	0.0	0.0
Breast ca.* (pl.ef) MCF-7	0.0	0.0	0.0
Breast ca.* (pl.ef) MDA-MB-231	0.0	18.9	40.6
Breast ca.* (pl. ef) T47D	0.0	0.0	0.0
Breast ca. BT-549	0.0	11.4	23.0
Breast ca. MDA-N	0.0	0.0	0.0
Ovary	0.0	0.0	0.0
Ovarian ca. OVCAR-3	0.0	0.0	0.0
Ovarian ca. OVCAR-4	17.4	0.0	0.0
Ovarian ca. OVCAR-5	55.1	32.1	44.1
Ovarian ca. OVCAR-8	0.0	26.1	0.0
Ovarian ca. IGROV-1	0.0	0.0	7.2
Ovarian ca. (ascites) SK-OV-3	0.0	0.0	32.3
Uterus	0.0	0.0	12.6
Placenta	0.0	18.9	12.2
Prostate	0.0	10.4	0.0
Prostate ca.* (bone met) PC-3	9.8	7.2	22.8
Testis	0.0	10.4	1.8
Melanoma Hs688(A).T	0.0	19.5	12.5
Melanoma* (met) Hs688(B).T	10.7	24.1	11.5
Melanoma UACC-62	0.0	55.5	12.9
Melanoma M14	0.0	0.0	0.0
Melanoma LOX IMVI	0.0	0.0	0.0
Melanoma* (met) SK-MEL-5	0.0	0.0	0.0
Adipose	0.0	0.0	11.6

Table DG. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag2433, Run 174477016	Rel. Exp.(%) Ag2479, Run 174924059	Tissue Name	Rel. Exp.(%) Ag2433, Run 174477016	Rel. Exp.(%) Ag2479, Run 174924059
Normal Colon	6.4	29.9	Kidney Margin (OD04348)	26.1	66.9
Colon cancer (OD06064)	0.0	0.0	Kidney malignant	10.8	10.4

			cancer (OD06204B)		
Colon Margin (OD06064)	0.0	5.9	Kidney normal adjacent tissue (OD06204E)	0.0	14.7
Colon cancer (OD06159)	0.0	0.0	Kidney Cancer (OD04450-01)	2.2	20.2
Colon Margin (OD06159)	16.7	9.1	Kidney Margin (OD04450-03)	7.6	14.6
Colon cancer (OD06297-04)	0.0	0.0	Kidney Cancer 8120613	0.0	0.0
Colon Margin (OD06297-015)	9.3	9.5	Kidney Margin 8120614	6.7	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	6.3	Kidney Cancer 9010320	13.8	9.5
CC Margin (ODO3921)	0.0	0.0	Kidney Margin 9010321	5.1	47.0
Colon cancer metastasis (OD06104)	0.0	0.0	Kidney Cancer 8120607	0.0	0.0
Lung Margin (OD06104)	0.0	0.0	Kidney Margin 8120608	0.0	7.6
Colon mets to lung (OD04451-01)	15.6	17.0	Normal Uterus	19.5	49.3
Lung Margin (OD04451-02)	27.4	34.6	Uterine Cancer 064011	0.0	14.7
Normal Prostate	6.3	19.6	Normal Thyroid	0.0	29.9
Prostate Cancer (OD04410)	0.0	18.8	Thyroid Cancer	0.0	0.0
Prostate Margin (OD04410)	6.7	9.3	Thyroid Cancer A302152	0.0	0.0
Normal Ovary	0.0	11.8	Thyroid Margin A302153	5.7	0.0
Ovarian cancer (OD06283-03)	8.0	16.4	Normal Breast	31.9	33.9
Ovarian Margin (OD06283-07)	16.4	10.4	Breast Cancer	15.3	37.6
Ovarian Cancer	31.2	0.0	Breast Cancer	**100.0**	**100.0**
Ovarian cancer (OD06145)	0.0	0.0	Breast Cancer (OD04590-01)	48.6	15.0
Ovarian Margin (OD06145)	46.0	58.6	Breast Cancer Mets	7.4	21.3

			(OD04590-03)		
Ovarian cancer (OD06455-03)	0.0	32.3	Breast Cancer Metastasis	67.8	85.3
Ovarian Margin (OD06455-07)	11.7	6.4	Breast Cancer	7.9	38.7
Normal Lung	12.9	0.0	Breast Cancer 9100266	0.0	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	0.0	Breast Margin 9100265	0.0	0.0
Lung Margin (ODO4945-03)	7.5	22.4	Breast Cancer A209073	0.0	9.8
Lung Malignant Cancer (OD03126)	0.0	0.0	Breast Margin A2090734	13.8	59.9
Lung Margin (OD03126)	22.7	0.0	Breast cancer (OD06083)	33.9	52.1
Lung Cancer (OD05014A)	6.5	20.3	Breast cancer node metastasis (OD06083)	14.8	29.3
Lung Margin (OD05014B)	18.2	0.0	Normal Liver	10.7	27.5
Lung cancer (OD06081)	14.3	8.8	Liver Cancer 1026	0.0	0.0
Lung Margin (OD06081)	0.0	15.1	Liver Cancer 1025	15.8	27.4
Lung Cancer (OD04237-01)	11.0	8.5	Liver Cancer 6004-T	13.3	3.6
Lung Margin (OD04237-02)	22.2	18.9	Liver Tissue 6004-N	0.0	3.7
Ocular Mel Met to Liver (ODO4310)	12.7	9.2	Liver Cancer 6005-T	12.6	0.0
Liver Margin (ODO4310)	0.0	5.5	Liver Tissue 6005-N	7.9	0.0
Melanoma Metastasis	0.0	0.0	Liver Cancer	13.8	48.0
Lung Margin (OD04321)	0.0	0.0	Normal Bladder	0.0	20.6
Normal Kidney	7.4	15.8	Bladder Cancer	0.0	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	24.3	8.5	Bladder Cancer	0.0	0.0
Kidney Margin	0.0	0.0	Normal	16.0	39.0

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(OD04338)			Stomach		
Kidney Ca Nuclear grade ½ (OD04339)	0.0	39.8	Gastric Cancer 9060397	0.0	0.0
Kidney Margin (OD04339)	11.9	9.9	Stomach Margin 9060396	0.0	20.0
Kidney Ca, Clear cell type (OD04340)	0.0	0.0	Gastric Cancer 9060395	32.5	9.6
Kidney Margin (OD04340)	7.0	6.0	Stomach Margin 9060394	0.0	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	0.0	Gastric Cancer 064005	16.0	30.8

Table DH. Panel 2D

Tissue Name	Rel. Exp.(%) Ag2201, Run 164025338	Tissue Name	Rel. Exp.(%) Ag2201, Run 164025338
Normal Colon	22.7	Kidney Margin 8120608	1.1
CC Well to Mod Diff (ODO3866)	7.5	Kidney Cancer 8120613	0.0
CC Margin (ODO3866)	1.4	Kidney Margin 8120614	4.8
CC Gr.2 rectosigmoid (ODO3868)	1.0	Kidney Cancer 9010320	7.4
CC Margin (ODO3868)	0.0	Kidney Margin 9010321	28.9
CC Mod Diff (ODO3920)	1.9	Normal Uterus	0.0
CC Margin (ODO3920)	6.8	Uterine Cancer 064011	18.3
CC Gr.2 ascend colon (ODO3921)	7.9	Normal Thyroid	3.0
CC Margin (ODO3921)	2.0	Thyroid Cancer	0.0
CC from Partial Hepatectomy (ODO4309) Mets	0.9	Thyroid Cancer A302152	1.5
Liver Margin (ODO4309)	1.7	Thyroid Margin A302153	7.1
Colon mets to lung	4.3	Normal Breast	20.4

(OD04451-01)			
Lung Margin (OD04451-02)	3.5	Breast Cancer	10.3
Normal Prostate 6546-1	5.0	Breast Cancer (OD04590-01)	14.5
Prostate Cancer (OD04410)	15.5	Breast Cancer Mets (OD04590-03)	34.4
Prostate Margin (OD04410)	8.8	Breast Cancer Metastasis	69.7
Prostate Cancer (OD04720-01)	12.0	Breast Cancer	30.8
Prostate Margin (OD04720-02)	17.2	Breast Cancer	**100.0**
Normal Lung	6.9	Breast Cancer 9100266	11.7
Lung Met to Muscle (ODO4286)	4.2	Breast Margin 9100265	6.8
Muscle Margin (ODO4286)	4.4	Breast Cancer A209073	12.2
Lung Malignant Cancer (OD03126)	3.2	Breast Margin A2090734	8.9
Lung Margin (OD03126)	10.5	Normal Liver	10.4
Lung Cancer (OD04404)	1.0	Liver Cancer	5.6
Lung Margin (OD04404)	10.4	Liver Cancer 1025	2.6
Lung Cancer (OD04565)	3.7	Liver Cancer 1026	2.1
Lung Margin (OD04565)	16.5	Liver Cancer 6004-T	3.0
Lung Cancer (OD04237-01)	3.0	Liver Tissue 6004-N	3.9
Lung Margin (OD04237-02)	4.3	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	4.5	Liver Tissue 6005-N	0.7
Liver Margin (ODO4310)	2.0	Normal Bladder	2.6
Melanoma Metastasis	0.0	Bladder Cancer	6.2
Lung Margin (OD04321)	2.6	Bladder Cancer	13.8
Normal Kidney	20.3	Bladder Cancer (OD04718-01)	1.8
Kidney Ca, Nuclear grade 2 (OD04338)	1.0	Bladder Normal Adjacent (OD04718-03)	5.0
Kidney Margin (OD04338)	2.8	Normal Ovary	0.7

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Kidney Ca Nuclear grade ½ (OD04339)	9.2	Ovarian Cancer	3.8
Kidney Margin (OD04339)	18.8	Ovarian Cancer (OD04768-07)	6.7
Kidney Ca, Clear cell type (OD04340)	15.4	Ovary Margin (OD04768-08)	0.0
Kidney Margin (OD04340)	22.7	Normal Stomach	14.5
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 9060358	0.0
Kidney Margin (OD04348)	5.2	Stomach Margin 9060359	2.1
Kidney Cancer (OD04622-01)	1.9	Gastric Cancer 9060395	1.4
Kidney Margin (OD04622-03)	0.0	Stomach Margin 9060394	6.0
Kidney Cancer (OD04450-01)	10.3	Gastric Cancer 9060397	5.6
Kidney Margin (OD04450-03)	13.9	Stomach Margin 9060396	4.4
Kidney Cancer 8120607	0.7	Gastric Cancer 064005	27.7

Table DI. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2201, Run 161905857	Rel. Exp.(%) Ag2433, Run 164183915	Rel. Exp.(%) Ag2479, Run 164391870	Rel. Exp.(%) Ag2537, Run 164321131
Secondary Th1 act	2.6	2.1	7.4	9.4
Secondary Th2 act	55.1	16.7	29.1	16.3
Secondary Tr1 act	25.0	21.8	39.2	53.6
Secondary Th1 rest	5.7	1.8	20.2	10.1
Secondary Th2 rest	13.5	19.5	8.0	24.8
Secondary Tr1 rest	24.8	7.8	33.0	12.7
Primary Th1 act	18.8	9.7	10.3	3.0
Primary Th2 act	24.7	18.3	20.2	17.3
Primary Tr1 act	27.9	18.4	8.6	14.2
Primary Th1 rest	**100.0**	**100.0**	35.1	**100.0**
Primary Th2 rest	72.2	29.7	40.3	44.8
Primary Tr1 rest	17.3	0.0	21.3	17.6
CD45RA CD4 lymphocyte act	14.6	4.1	16.3	15.9
CD45RO CD4	26.4	17.6	33.4	6.3

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lymphocyte act				
CD8 lymphocyte act	24.0	24.5	40.9	14.2
Secondary CD8 lymphocyte rest	25.5	51.8	42.6	26.6
Secondary CD8 lymphocyte act	10.2	4.8	5.5	6.7
CD4 lymphocyte none	8.8	5.2	12.4	5.1
2ry Th1/Th2/Tr1_anti-CD95 CH11	32.1	12.2	9.3	5.8
LAK cells rest	5.0	2.6	10.6	3.9
LAK cells IL-2	59.9	33.2	71.7	39.8
LAK cells IL-2+IL-12	31.2	32.8	37.9	54.0
LAK cells IL-2+IFN gamma	11.3	37.4	36.1	56.6
LAK cells IL-2+ IL-18	23.5	29.1	40.9	22.7
LAK cells PMA/ionomycin	0.0	2.5	7.2	5.1
NK Cells IL-2 rest	17.3	21.5	39.8	19.3
Two Way MLR 3 day	92.0	62.0	**100.0**	62.0
Two Way MLR 5 day	32.8	20.3	26.4	30.8
Two Way MLR 7 day	18.6	8.6	17.6	16.3
PBMC rest	8.4	2.4	0.0	7.5
PBMC PWM	37.4	26.1	70.2	45.7
PBMC PHA-L	6.0	8.6	24.8	14.6
Ramos (B cell) none	25.2	11.0	20.4	7.5
Ramos (B cell) ionomycin	41.8	35.4	44.8	45.7
B lymphocytes PWM	17.6	2.0	8.3	20.2
B lymphocytes CD40L and IL-4	21.5	17.3	16.8	25.3
EOL-1 dbcAMP	2.7	0.0	0.0	0.0
EOL-1 dbcAMP PMA/ionomycin	4.7	7.0	0.0	0.0
Dendritic cells none	13.4	1.8	16.7	14.7
Dendritic cells LPS	10.7	14.2	2.4	11.6
Dendritic cells anti-CD40	12.5	12.2	10.4	3.0
Monocytes rest	2.5	0.0	7.7	4.3
Monocytes LPS	12.7	18.8	25.0	10.0
Macrophages rest	8.3	7.9	11.0	10.9
Macrophages LPS	3.2	3.8	6.3	0.0
HUVEC none	3.1	2.3	0.0	3.7

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HUVEC starved	8.7	4.6	11.4	6.9
HUVEC IL-1beta	2.4	5.2	5.5	0.6
HUVEC IFN gamma	15.8	13.6	33.0	21.2
HUVEC TNF alpha + IFN gamma	0.0	0.0	4.7	0.0
HUVEC TNF alpha + IL4	11.4	0.0	8.4	0.0
HUVEC IL-11	0.0	4.8	19.5	5.4
Lung Microvascular EC none	29.9	14.4	25.7	12.8
Lung Microvascular EC TNFalpha + IL-1beta	26.1	25.7	18.4	25.9
Microvascular Dermal EC none	3.3	2.0	3.1	3.9
Microsvasular Dermal EC TNFalpha + IL-1beta	6.5	0.0	10.7	8.9
Bronchial epithelium TNFalpha + IL1beta	16.2	16.3	11.8	15.7
Small airway epithelium none	8.2	5.7	9.2	0.0
Small airway epithelium TNFalpha + IL-1beta	31.2	23.8	39.0	32.5
Coronery artery SMC rest	0.0	12.6	3.2	1.3
Coronery artery SMC TNFalpha + IL-1beta	0.0	6.4	0.0	6.1
Astrocytes rest	2.7	0.0	5.7	2.9
Astrocytes TNFalpha + IL-1beta	3.3	10.7	0.0	8.1
KU-812 (Basophil) rest	0.0	6.6	3.3	3.4
KU-812 (Basophil) PMA/ionomycin	0.0	5.5	8.3	3.3
CCD1106 (Keratinocytes) none	6.7	7.2	3.4	7.0
CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	20.9	3.6	0.0
Liver cirrhosis	26.2	22.5	39.5	15.3
Lupus kidney	1.6	2.5	9.9	3.3
NCI-H292 none	10.8	6.7	10.0	12.0
NCI-H292 IL-4	16.6	17.4	13.3	16.7

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NCI-H292 IL-9	5.4	5.6	4.9	16.6
NCI-H292 IL-13	6.6	0.0	0.0	6.8
NCI-H292 IFN gamma	2.9	5.4	6.8	0.0
HPAEC none	6.4	0.0	4.5	2.7
HPAEC TNF alpha + IL-1 beta	8.5	9.9	19.8	3.1
Lung fibroblast none	0.0	5.5	2.0	9.0
Lung fibroblast TNF alpha + IL-1 beta	11.7	0.0	0.0	0.0
Lung fibroblast IL-4	16.8	8.7	22.7	11.2
Lung fibroblast IL-9	9.4	8.2	3.3	6.2
Lung fibroblast IL-13	5.0	13.2	1.5	2.5
Lung fibroblast IFN gamma	19.8	7.1	19.3	19.1
Dermal fibroblast CCD1070 rest	26.6	26.1	35.1	13.9
Dermal fibroblast CCD1070 TNF alpha	40.3	19.3	31.2	21.0
Dermal fibroblast CCD1070 IL-1 beta	13.0	10.0	18.0	15.7
Dermal fibroblast IFN gamma	19.3	9.8	11.2	21.3
Dermal fibroblast IL-4	25.7	2.0	36.1	28.5
IBD Colitis 2	10.9	6.3	2.4	0.0
IBD Crohn's	0.0	0.0	7.5	2.5
Colon	6.5	15.8	20.2	12.9
Lung	32.5	16.5	24.8	23.8
Thymus	16.2	5.6	28.5	20.7
Kidney	13.7	18.2	21.8	10.4

CNS_neurodegeneration_v1.0 Summary: <u>Ag2479/Ag2537/Ag2201</u> The GMAC004977_A gene is expressed primarily in the cerebellum and also shows increased expression in the hippocampus and inferior temporal cortex of some brains affected with Alzheimer's disease when compared to normal baseline expression in unaffected brains. The hippocampus is an important anatomical focus of Alzheimer's pathology, indicating that the GMAC004977_A gene product may be an important biochemical component of the disease. GPCRs are readily targetable with drugs, and regulate many specific brain processes, including signaling processes that are currently the target of FDA-approved pharmaceuticals that treat Alzheimer's disease, such as the cholinergic system. The major mechanisms proposed for Abeta-induced cytotoxicity involve the loss of Ca2+ homeostasis and the generation of

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reactive oxygen species (ROS). The changes in Ca2+ homeostasis could be the result of changes in G-protein-driven releases of second messengers. Thus, targeting this class of molecule can have therapeutic potential in Alzheimer's disease treatment. In particular, the increased expression of the GMAC004977_A gene in some brains affected by Alzheimer's

5   indicates potential therapeutic value to drugs that target this GPCR. Normal expression of this gene in the cerebellum suggests that this GPCR may also be effectively targeted to treat diseases involving the cerebellum, including spinocerebellar ataxias, batten disease, and Niemann-Pick disease. Data from one run with Ag2433, Run 228396997, is not included because the amp plot suggests experimental problems (data not shown).

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    Panel 1.3D Summary: Ag2479/Ag2537/Ag2201 Results from three experiments using different probe/primer sets show somewhat disparate results, most likely because the levels of gene expression are very low in this panel. Using Ag2201 and Ag2537, expression of the GMAC004977_A gene is highest in a brain cancer cell line (CT=34). In addition, there is low

15   but significant expression in an additional sample derived from a brain cancer cell line. Other apparent expression is below the level of reliable evaluation. Of note is the observation that both of the cell lines showing substantial GMAC004977_A gene expression are derived from a type of brain cancer called glioblastoma. Thus, the expression of this gene could be used to distinguish between glioblastoma derived samples and other samples. Moreover, therapeutic

20   modulation of the expression or function of the GMAC004977_A gene or its protein product, through the use of small molecule drugs, antibodies or protein therapeutics might be of use in the treatment of glioblastoma. Using Ag2479, expression is highest in spleen (CT=34), with low but significant expression also seen in a melanoma cell line as well as a brain cancer cell line. Other apparent expression is below the level of reliable evaluation. Thus, therapeutic

25   modulation of the expression or function of this gene, through the use of small molecule drugs, antibodies or protein therapeutics might be of use in the treatment of brain cancer or melanoma. Ag2433 Expression of this gene in panel 1.3D is low/undetectable (CT values >35) in all samples (data not shown).

30   **Panel 2.2 Summary:** Ag2479/Ag2433 Two experiments with two different probe and primer sets produce results that are in excellent agreement. In both runs, expression is limited to samples derived from breast cancer. Thus, expression of the GMAC004977_A gene could be used to distinguish samples derived from breast cancer from other samples. Moreover, therapeutic modulation of the expression or function of this gene or its protein product,

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through the use of small molecule drugs or antibodies, might be of use in the treatment of breast cancer.

Panel 2D Summary: Ag2201 Expression of the GMAC004977_A gene is highest in a sample derived from a breast cancer (CT = 30.1). In addition, a number of other breast cancer samples show substantial expression, including samples of cancer tissue with matched samples derived from normal adjacent tissue. In all these samples, the GMAC004977_A gene appears to be over-expressed in the cancerous tissue. This result agrees with the expression profile detected in Panel 2.2 and suggests that expression of this gene could be used to distinguish breast cancer tissue from other tissues, perhaps as a diagnostic marker for the presence of breast cancer. Moreover, therapeutic inhibition of the protein encoded by the GMAC004977_A gene may be effective in the treatment of breast cancer.

Panel 4D Summary: Ag2479/Ag2537/Ag2201/Ag2433 The GMAC004977_A gene is expressed in Panel 4D at moderate to low levels in numerous independent preparations of activated B cells, resting and activated T cells, and activated lymphokine-activated killer cells. This pattern of restricted expression suggests that specific antibodies and small molecule drugs that inhibit the function of the protein encoded by the GMAC004977_A gene may be useful in reducing or eliminating inflammation and autoimmune disease symptoms in patients with Crohn's disease, inflammatory bowel disease, asthma, psoriasis, and rheumatoid arthritis.

E. GMAP001804_H/CG145149-01: Olfactory Receptor

Expression of gene GMAP001804_H (also know as CG145149-01) was assessed using the primer-probe set Ag2216, described in Table EA. Results of the RTQ-PCR runs are shown in Tables EB and EC.

Table EA. Probe Name Ag2216

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atggaaagactgcattcaggta-3'	22	753	231
Probe	TET-5'-ttaaaacccgccataaccagttccct-3'-TAMRA	26	776	232
Reverse	5'-tagaacacagaggccacattct-3'	22	810	233

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Table EB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2216, Run 165974838	Tissue Name	Rel. Exp.(%) Ag2216, Run 165974838
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	16.6	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	10.4	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	14.3
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0

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Tissue	Rel. Exp.	Tissue	Rel. Exp.
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	45.1
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	12.6
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	23.8
Colon ca.* SW620 (SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	45.4
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	**100.0**
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table EC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2216, Run 163724265	Tissue Name	Rel. Exp.(%) Ag2216, Run 163724265
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0

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Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	12.7	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	14.7	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	13.7	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0

Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	12.9
PBMC PWM	12.6	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	11.5
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	38.7	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	29.3
Dendritic cells anti-CD40	23.7	IBD Colitis 2	27.4
Monocytes rest	0.0	IBD Crohn's	12.6
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	22.7	Lung	12.2
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	12.2		

Panel 1.3D Summary: Ag2216 Significant expression of the GMAP001804_H gene is seen exclusively in melanoma cell line UACC-62 (CT = 34.7). Therefore, expression of this gene may be used to distinguish this melanoma cell line from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of melanoma.

Panel 2.2 Summary: Ag2216 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag2216 Significant expression of the GMAP001804_H gene is detected in a liver cirrhosis sample (CT = 34.3). Furthermore, expression of this gene is not

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detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

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F. GMAC005143_A/CG143809-01: Olfactory Receptor

Expression of gene GMAC005143_A (also known as CG143809-01) was assessed using the primer-probe set Ag2208, described in Table FA. Results of the RTQ-PCR runs are shown in Table FB.

10   Table FA. Probe Name Ag2208

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atacaaatgtggttcccatgtt-3'	22	834	234
Probe	TET-5'-ccccttaatctacagcctgaggaaca-3'-TAMRA	26	859	235
Reverse	5'-ggcttttcttagggcaaattta-3'	22	892	236

Table FB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2208, Run 165974834	Tissue Name	Rel. Exp.(%) Ag2208, Run 165974834
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	21.6
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0

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Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	15.8
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
Glioma U251	34.6	Breast ca.* (pl.ef) MCF-7	47.6
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	38.7
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	15.2	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	14.0
Colon ca.* SW620 (SW480 met)	0.0	Prostate	0.0

Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	15.2
Colon ca. HCT-116	0.0	Testis	28.9
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	**100.0**
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Panel 1.3D Summary: Ag2208 Expression of the GMAC005143_A gene is highest in a sample derived from melanoma cell line UACC-62 (CT = 33.5). In addition, there is significant expression in two breast cancer cell lines (MCF-7 and T47D). Thus, the expression of this gene could be used to distinguish these samples from other samples in the panel. Moreover, therapeutic modulation of this gene or its protein product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of breast cancer or melanoma.

Panel 2.2 Summary: Ag2208 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag2208 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

G. GMAP001804_J, GMAP001804_G, and GMAP001804_C: Olfactory Receptor

Expression of genes GMAP001804_J, GMAP001804_G, and GMAP001804_C was assessed using the primer-probe sets Ag2208, Ag2218 and Ag2360, described in Tables GA, GB, and GC. Results of the RTQ-PCR runs are shown in Tables GD and GE.

Table GA. Probe Name Ag2208

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atacaaatgtggttcccatgtt-3'	22	834	237
Probe	TET-5'-ccccttaatctacagcctgaggaaca-3'-TAMRA	26	859	238
Reverse	5'-ggcttttcttagggcaaattta-3'	22	892	239

Table GB. Probe Name Ag2218

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggctgaactcacaccttcatac-3'	22	150	576
Probe	TET-5'-ccccatgtacttcttcctctttaacttg-3'-TAMRA	28	172	577
Reverse	5'-tagcattttgggtgtaaacaca-3'	22	226	578

Table GC. Probe Name Ag2360

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggctgaactcacaccttcatac-3'	22	150	579
Probe	TET-5'-ccccatgtacttcttcctctttaacttg-3'-TAMRA	28	172	580
Reverse	5'-tagcattttgggtgtaaacaca-3'	22	226	581

Table GD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2208, Run 165974834	Tissue Name	Rel. Exp.(%) Ag2208, Run 165974834
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	21.6
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0

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Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	15.8
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	34.6	Breast ca.* (pl.ef) MCF-7	47.6
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	38.7
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	15.2	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	14.0

Colon ca.* SW620 (SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	15.2
Colon ca. HCT-116	0.0	Testis	28.9
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	**100.0**
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table GE. Panel 2D

Tissue Name	Rel. Exp.(%) Ag2360, Run 164158100	Tissue Name	Rel. Exp.(%) Ag2360, Run 164158100
Normal Colon	11.2	Kidney Margin 8120608	0.0
CC Well to Mod Diff (ODO3866)	0.0	Kidney Cancer 8120613	0.0
CC Margin (ODO3866)	11.7	Kidney Margin 8120614	0.0
CC Gr.2 rectosigmoid (ODO3868)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3868)	0.0	Kidney Margin 9010321	0.0
CC Mod Diff (ODO3920)	0.0	Normal Uterus	0.0
CC Margin (ODO3920)	0.0	Uterine Cancer 064011	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Normal Thyroid	0.0
CC Margin (ODO3921)	0.0	Thyroid Cancer	0.0
CC from Partial Hepatectomy (ODO4309) Mets	0.0	Thyroid Cancer A302152	0.0
Liver Margin	0.0	Thyroid Margin	0.0

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(ODO4309)		A302153	
Colon mets to lung (OD04451-01)	0.0	Normal Breast	0.0
Lung Margin (OD04451-02)	0.0	Breast Cancer	3.5
Normal Prostate 6546-1	0.0	Breast Cancer (OD04590-01)	0.0
Prostate Cancer (OD04410)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Prostate Margin (OD04410)	0.0	Breast Cancer Metastasis	0.0
Prostate Cancer (OD04720-01)	0.0	Breast Cancer	0.0
Prostate Margin (OD04720-02)	4.5	Breast Cancer	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Lung Met to Muscle (ODO4286)	14.2	Breast Margin 9100265	0.0
Muscle Margin (ODO4286)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.0	Normal Liver	0.0
Lung Cancer (OD04404)	0.0	Liver Cancer	17.3
Lung Margin (OD04404)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04565)	2.8	Liver Cancer 1026	0.0
Lung Margin (OD04565)	0.0	Liver Cancer 6004-T	0.0
Lung Cancer (OD04237-01)	7.6	Liver Tissue 6004-N	0.0
Lung Margin (OD04237-02)	0.0	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	0.0	Normal Bladder	0.0
Melanoma Metastasis	0.0	Bladder Cancer	0.0
Lung Margin (OD04321)	0.0	Bladder Cancer	**100.0**
Normal Kidney	0.0	Bladder Cancer (OD04718-01)	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	7.4	Bladder Normal Adjacent (OD04718-03)	0.0

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Kidney Margin (OD04338)	0.0	Normal Ovary	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	15.7	Ovarian Cancer	0.0
Kidney Margin (OD04339)	0.0	Ovarian Cancer (OD04768-07)	2.8
Kidney Ca, Clear cell type (OD04340)	0.0	Ovary Margin (OD04768-08)	0.0
Kidney Margin (OD04340)	0.0	Normal Stomach	7.3
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 9060358	0.0
Kidney Margin (OD04348)	0.0	Stomach Margin 9060359	0.0
Kidney Cancer (OD04622-01)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04622-03)	0.0	Stomach Margin 9060394	0.0
Kidney Cancer (OD04450-01)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04450-03)	0.0	Stomach Margin 9060396	0.0
Kidney Cancer 8120607	0.0	Gastric Cancer 064005	0.0

CNS_neurodegeneration_v1.0 Summary: Ag2360 Expression of this gene is low/undetectable (CTs >35) across all samples in this panel (data not shown).

Panel 1.3D Summary: Ag2208 Expression of the GMAP001804_J gene is highest in a sample derived from melanoma cell line UACC-62 (CT = 33.5). In addition, there is significant expression in two breast cancer cell lines (MCF-7 and T47D). Thus, the expression of this gene could be used to distinguish these samples from other samples in the panel. Moreover, therapeutic modulation of this gene or its protein product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of breast cancer or melanoma. Ag2218 Results from one experiment using this probe/primer set are not included because there were experimental problems with one of the wells (data not shown). Ag2360 Expression of this gene is low/undetectable (CTs >35) across all samples in this panel (data not shown).

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Panel 2.2 Summary: Ag2208 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown). Ag2218/Ag2360 Data from these experiments are not included because there was a high probability chemistry failure (data not shown).

Panel 2D Summary: Ag2360 Low but significant expression of the GMAP001804_J gene is limited to a single bladder cancer sample (CT = 34.4). Therefore, expression of this gene may be used as a marker for bladder cancer. Furthermore, therapeutic modulation of the activity of this gene product may be beneficial in the treatment of bladder cancer.

Panel 3D Summary: Ag2360 Expression of this gene is low/undetectable (CTs >35) across all samples in this panel (data not shown).

Panel 4D Summary: Ag2208/Ag2218/Ag2360 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

H. GMAP001804_B/CG54353-01: OLFACTORY RECEPTOR

Expression of gene GMAP001804_B (also known as CG54353-01) was assessed using the primer-probe sets Ag3091 and Ag2549, described in Tables HA and HB. Results of the RTQ-PCR runs are shown in Tables HC, HD, HE and HF.

Table HA. Probe Name Ag3091

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggtgcatgactcagctgttt-3'	20	294	240
Probe	TET-5'-tcatctctgaatgttacatgttgacctca-3'-TAMRA	29	330	241
Reverse	5'-gccacatagcgatcatatgc-3'	20	362	242

Table HB. Probe Name Ag2549

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tctcacctccacacaccaat-3'	20	164	243
Probe	TET-5'-ttcctcttcaatctctccttcattga-3'-TAMRA	26	191	244
Reverse	5'-gcattttgggagtgaaaaca-3'	20	232	245

Table HC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3091, Run 167985245	Tissue Name	Rel. Exp.(%) Ag3091, Run 167985245
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	1.6
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	8.1	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	2.2
glio/astro U-118-MG	4.7	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	74.7
glioma SF-295	1.2	Breast ca.* (pl.ef) MDA-MB-231	0.0

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Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	**100.0**
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	15.7
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	5.5	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.0
Colon ca.* SW620 (SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	8.3
Colon ca. HCT-116	0.0	Testis	16.4
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	20.4
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table HD. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag3091, Run 174285051	Tissue Name	Rel. Exp.(%) Ag3091, Run 174285051
Normal Colon	0.0	Kidney Margin (OD04348)	0.0

Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	10.7
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	15.6
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	8.7	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	13.8
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer	0.0
Ovarian Cancer	4.1	Breast Cancer	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	22.8	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer	0.0

Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	11.3	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	0.0
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	4.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0
Liver Margin (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer	14.5
Lung Margin (OD04321)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	13.0	Bladder Cancer	**100.0**
Kidney Margin (OD04338)	14.8	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	5.4
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	15.0
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table HE. Panel 4.1D

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Tissue Name	Rel. Exp.(%) Ag2549, Run 224781632	Rel. Exp.(%) Ag3091, Run 175179976	Tissue Name	Rel. Exp.(%) Ag2549, Run 224781632	Rel. Exp.(%) Ag3091, Run 175179976
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	0.2	0.0
Secondary Tr1 act	0.0	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	0.2	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0
Primary Th1 rest	0.0	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	0.0	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0	0.0
CD45RA CD4 lymphocyte act	0.0	0.0	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.5
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8	0.0	0.0	Astrocytes	0.0	0.0

lymphocyte rest			TNFalpha + IL-1beta		
Secondary CD8 lymphocyte act	0.0	0.0	KU-812 (Basophil) rest	0.2	0.0
CD4 lymphocyte none	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	0.0	0.4
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	0.0	0.0	Liver cirrhosis	0.3	0.0
LAK cells IL-2+IL-12	0.0	0.0	NCI-H292 none	0.2	0.0
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 IL-4	0.0	0.0
LAK cells IL-2+IL-18	0.0	0.0	NCI-H292 IL-9	0.0	0.0
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-13	0.0	0.0
NK Cells IL-2 rest	0.0	0.0	NCI-H292 IFN gamma	0.0	0.0
Two Way MLR 3 day	0.0	0.0	HPAEC none	0.0	0.0
Two Way MLR 5 day	0.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	0.0
Two Way MLR 7 day	0.0	0.0	Lung fibroblast none	0.0	2.3
PBMC rest	0.0	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.2	0.0
PBMC PWM	0.0	0.0	Lung fibroblast IL-4	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-9	0.7	0.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes PWM	0.0	0.0	Dermal fibroblast CCD1070 rest	0.0	0.3

B lymphocytes CD40L and IL-4	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	0.0
EOL-1 dbcAMP	0.2	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast IFN gamma	0.4	0.0
Dendritic cells none	0.9	1.7	Dermal fibroblast IL-4	0.2	0.0
Dendritic cells LPS	0.2	0.0	Dermal Fibroblasts rest	0.6	0.0
Dendritic cells anti-CD40	0.4	5.1	Neutrophils TNFa+LPS	0.4	0.7
Monocytes rest	0.0	0.0	Neutrophils rest	1.1	3.1
Monocytes LPS	0.0	0.0	Colon	1.3	1.8
Macrophages rest	0.7	4.1	Lung	2.6	3.9
Macrophages LPS	0.0	0.0	Thymus	14.3	7.0
HUVEC none	0.0	0.0	Kidney	**100.0**	**100.0**
HUVEC starved	0.0	0.0			

Table HF. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3091, Run 164525694	Tissue Name	Rel. Exp.(%) Ag3091, Run 164525694
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0

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Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	17.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast	0.0

PMA/ionomycin		CCD1070 IL-1 beta	
Dendritic cells none	31.6	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	4.6	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	43.2	IBD Colitis 2	2.9
Monocytes rest	0.0	IBD Crohn's	7.6
Monocytes LPS	0.0	Colon	40.1
Macrophages rest	**100.0**	Lung	55.9
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

CNS_Neurodegeneration_v1.0 Summary: Ag2549 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag3091 The expression of the GMAP001804_B gene appears to be restricted to two breast cancer cell lines. Interestingly, both of these cell lines are positive for estrogen receptor expression. Thus, this gene may be a marker for estrogen receptor positive breast cancer cells. Further, therapeutic modulation of this gene may be of use in the treatment of breast cancer or other breast related diseases. Ag2549 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag3091 Two RTQ-PCR experiments were performed using probe/primer set Ag3091. In one experiment, AP001804_D gene expression was low to undetectable (CT values >35) in all samples (data not shown). In the other experiment, expression was low/undectable in all samples except a single bladder cancer cell line (CT=34.5). Expression levels are too low for reliable analysis. Ag2549 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4.1D Summary: Ag2549 The GMAP001804_B gene is expressed at detectable levels in the kidney with lower expression in the thymus. The putative GPCR encoded for by this gene could allow cells within the kidney to respond to specific microenvironmental signals. Therefore, antibody or small molecule therapies designed with the protein encoded for by this gene could modulate kidney function and be important in the treatment of inflammatory or autoimmune diseases that affect the kidney, including lupus and glomerulonephritis. Please

note that data from a second experiment with the same probe and primer set showed low/undetectable levels of expression in all the samples in this panel (Data not shown).

Panel 4D Summary: Ag1639 The GMAP001804_B transcript is detectable in resting macrophages and not at significant levels in other cell types. The putative GPCR encoded for by this transcript may therefore be important in macrophage detection of chemokine gradients and trafficking into specific sites within a tissue and in activation. Antibody or protein therapeutics designed against the AP001804_D protein encoded for by this transcript could reduce or inhibit inflammation in asthma, emphysema, allergy, psoriasis, arthritis, or any other condition in which macrophage localization/activation is important.

I. GMAC011711_I/CG152295-01: Olfactory Receptor

Expression of gene GMAC011711_I (also known as CG152295-01) was assessed using the primer-probe set Ag2352, described in Table IA. Results of the RTQ-PCR runs are shown in Tables IB and IC.

Table IA. Probe Name Ag2352

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ttttgcaaagtcaatgtcccttt-3'	22	514	246
Probe	TET-5'-attcttactgcttccaccctgatgcg-3'-TAMRA	26	539	247
Reverse	5'-agctgttcatccttgaatcaga-3'	22	580	248

Table IB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2352, Run 165974846	Tissue Name	Rel. Exp.(%) Ag2352, Run 165974846
Liver adenocarcinoma	1.5	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0

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Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	3.2	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	57.8
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	**100.0**
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
Glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
Glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	3.4
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	6.3
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	42.0
Glioma SNB-19	0.0	Mammary gland	0.0
Glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
Glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	3.3	Breast ca.* (pl. ef) T47D	0.0
Heart	1.7	Breast ca. BT-549	4.3
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	2.7
Lymph node	3.8	Ovarian ca.	0.0

		OVCAR-8	
Colorectal	0.0	Ovarian ca. IGROV-1	3.4
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	4.3
Small intestine	0.0	Uterus	1.0
Colon ca. SW480	0.0	Placenta	3.9
Colon ca.* SW620 (SW480 met)	0.0	Prostate	3.9
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	4.7	Melanoma* (met) SK-MEL-5	0.0
Kidney	1.5	Adipose	0.0

Table IC. Panel 2D

Tissue Name	Rel. Exp.(%) Ag2352, Run 164148259	Tissue Name	Rel. Exp.(%) Ag2352, Run 164148259
Normal Colon	4.1	Kidney Margin 8120608	0.7
CC Well to Mod Diff (ODO3866)	1.8	Kidney Cancer 8120613	4.8
CC Margin (ODO3866)	0.8	Kidney Margin 8120614	0.0
CC Gr.2 rectosigmoid (ODO3868)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3868)	0.0	Kidney Margin 9010321	0.0
CC Mod Diff (ODO3920)	0.0	Normal Uterus	1.3
CC Margin (ODO3920)	0.0	Uterine Cancer 064011	0.0

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CC Gr.2 ascend colon (ODO3921)	0.0	Normal Thyroid	0.0
CC Margin (ODO3921)	2.0	Thyroid Cancer	0.0
CC from Partial Hepatectomy (ODO4309) Mets	0.0	Thyroid Cancer A302152	0.5
Liver Margin (ODO4309)	0.0	Thyroid Margin A302153	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Breast	0.0
Lung Margin (OD04451-02)	0.0	Breast Cancer	0.0
Normal Prostate 6546-1	**100.0**	Breast Cancer (OD04590-01)	0.0
Prostate Cancer (OD04410)	85.3	Breast Cancer Mets (OD04590-03)	0.0
Prostate Margin (OD04410)	48.3	Breast Cancer Metastasis	0.0
Prostate Cancer (OD04720-01)	20.3	Breast Cancer	0.0
Prostate Margin (OD04720-02)	25.7	Breast Cancer	0.4
Normal Lung	0.0	Breast Cancer 9100266	1.4
Lung Met to Muscle (ODO4286)	2.7	Breast Margin 9100265	0.0
Muscle Margin (ODO4286)	0.0	Breast Cancer A209073	0.7
Lung Malignant Cancer (OD03126)	19.2	Breast Margin A2090734	0.0
Lung Margin (OD03126)	1.3	Normal Liver	0.8
Lung Cancer (OD04404)	0.0	Liver Cancer	0.0
Lung Margin (OD04404)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04565)	0.0	Liver Cancer 1026	0.8
Lung Margin (OD04565)	0.0	Liver Cancer 6004-T	0.0
Lung Cancer (OD04237-01)	0.0	Liver Tissue 6004-N	2.0
Lung Margin (OD04237-02)	1.6	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	0.6	Normal Bladder	0.7
Melanoma Metastasis	0.0	Bladder Cancer	0.0

Lung Margin (OD04321)	0.8	Bladder Cancer	3.2
Normal Kidney	0.0	Bladder Cancer (OD04718-01)	1.2
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Normal Adjacent (OD04718-03)	0.0
Kidney Margin (OD04338)	0.8	Normal Ovary	0.0
Kidney Ca Nuclear grade ½ (OD04339)	0.0	Ovarian Cancer	0.0
Kidney Margin (OD04339)	0.0	Ovarian Cancer (OD04768-07)	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Ovary Margin (OD04768-08)	0.0
Kidney Margin (OD04340)	0.0	Normal Stomach	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 9060358	0.0
Kidney Margin (OD04348)	0.6	Stomach Margin 9060359	0.0
Kidney Cancer (OD04622-01)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04622-03)	0.0	Stomach Margin 9060394	0.0
Kidney Cancer (OD04450-01)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04450-03)	0.0	Stomach Margin 9060396	0.0
Kidney Cancer 8120607	0.0	Gastric Cancer 064005	0.0

Panel 1.3D Summary: Ag2352 Low but significant expression of the GMAC011711_I gene is detected in three lung cancer cell lines (CTs = 33.2-34.5). Therefore, expression of this gene may be used to distinguish lung cancer cell lines from the other samples on this panel. Furthermore, therapeutic modulation of the activity of this gene product may be beneficial for the treatment of lung cancer.

Panel 2D Summary: Ag2352 Expression of the GMAC011711_I gene appears to be highest in a sample of normal prostate tissue (CT = 31.1). It also appears that the expression of this gene is limited to tissues, normal or malignant, derived from prostate. Thus, the expression of this gene could be used to distinguish prostate derived tissue from other tissues in the panel.

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Moreover, therapeutic modulation of this gene or its protein product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of prostate cancer.

5   **Panel 4D Summary:** Ag2352 Expression is low/undetectable (CTs > 35) across all of the samples on this panel.

J. GMAC009642_C/CG152495-01: Olfactory Receptor

Expression of gene GMAC009642_C (also known as CG152495-01) was assessed
10   using the primer-probe set Ag2341, described in Table JA. Results of the RTQ-PCR runs are shown in Tables JB, JC, and JD.

Table JA. Probe Name Ag2341

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gattccaggtttagaggaaagc-3'	22	107	249
Probe	TET-5'-cctgggcatcctttacctccttgctt-3'-TAMRA	26	149	250
Reverse	5'-agaatggtaacattgcccacta-3'	22	175	251

Table JB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2341, Run 207929091	Tissue Name	Rel. Exp.(%) Ag2341, Run 207929091
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	0.0
AD 2 Hippo	18.2	Control (Path) 4 Temporal Ctx	36.9
AD 3 Hippo	0.0	AD 1 Occipital Ctx	7.7
AD 4 Hippo	0.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	72.7	AD 3 Occipital Ctx	0.0
AD 6 Hippo	54.7	AD 4 Occipital Ctx	6.3
Control 2 Hippo	0.0	AD 5 Occipital Ctx	0.0
Control 4 Hippo	6.1	AD 5 Occipital Ctx	0.0
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	5.8
AD 1 Temporal Ctx	4.0	Control 2 Occipital	24.3

		Ctx	
AD 2 Temporal Ctx	29.1	Control 3 Occipital Ctx	14.7
AD 3 Temporal Ctx	1.7	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	10.8	Control (Path) 1 Occipital Ctx	35.4
AD 5 Inf Temporal Ctx	57.4	Control (Path) 2 Occipital Ctx	4.5
AD 5 Sup Temporal Ctx	32.1	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	31.6	Control (Path) 4 Occipital Ctx	40.6
AD 6 Sup Temporal Ctx	**100.0**	Control 1 Parietal Ctx	12.9
Control 1 Temporal Ctx	1.2	Control 2 Parietal Ctx	34.4
Control 2 Temporal Ctx	0.0	Control 3 Parietal Ctx	7.6
Control 3 Temporal Ctx	19.8	Control (Path) 1 Parietal Ctx	22.4
Control 3 Temporal Ctx	10.4	Control (Path) 2 Parietal Ctx	25.9
Control (Path) 1 Temporal Ctx	0.0	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	47.3	Control (Path) 4 Parietal Ctx	27.7

Table JC. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag2341, Run 174294736	Tissue Name	Rel. Exp.(%) Ag2341, Run 174294736
Normal Colon	94.0	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	70.7	Kidney malignant cancer (OD06204B)	38.4
Colon Margin (OD06064)	51.1	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer	0.0	Kidney Cancer	0.0

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(OD06297-04)		8120613	
Colon Margin (OD06297-015)	51.8	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	41.2	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	81.2
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	44.1
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	73.7	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer	0.0
Ovarian Cancer	66.9	Breast Cancer	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	33.7	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	57.0	Breast Cancer Metastasis	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	52.1
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	85.3

Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	81.2
Lung Margin (OD05014B)	0.0	Normal Liver	0.0
Lung cancer (OD06081)	26.6	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0
Liver Margin (ODO4310)	48.3	Liver Tissue 6005-N	60.3
Melanoma Metastasis	0.0	Liver Cancer	18.8
Lung Margin (OD04321)	18.2	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	33.9	Bladder Cancer	**100.0**
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	34.2	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	69.7
Kidney Margin (OD04340)	33.2	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table JD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2341, Run 164023038	Tissue Name	Rel. Exp.(%) Ag2341, Run 164023038
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	7.3	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0

Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	19.3
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	9.7	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	8.9
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	5.8	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	22.5
LAK cells IL-2+ IL-18	22.7	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0

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PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	9.9
Ramos (B cell) none	16.3	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	16.7
B lymphocytes PWM	9.5	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	7.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	11.2
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	18.7
Monocytes rest	98.6	IBD Crohn's	11.9
Monocytes LPS	10.2	Colon	25.0
Macrophages rest	0.0	Lung	32.1
Macrophages LPS	0.0	Thymus	23.8
HUVEC none	11.3	Kidney	7.8
HUVEC starved	11.9		

CNS_neurodegeneration_v1.0 **Summary**: <u>Ag2341</u> The GMAC009642_C gene is expressed at low levels in the brains of both normal and Alzheimer's disease patients and encodes a putative GPCR. Several neurotransmitter receptors are GPCRs, including the dopamine receptor family, the serotonin receptor family, the GABAB receptor, muscarinic

5   acetylcholine receptors, and others; thus this GPCR may represent a novel neurotransmitter receptor. Targeting various neurotransmitter receptors (dopamine, serotonin) has proven to be an effective therapy in psychiatric illnesses such as schizophrenia, bipolar disorder, and depression. Furthermore, the cerebral cortex and hippocampus are regions of the brain that are known to be involved in Alzheimer's disease, seizure disorders, and in the normal process

10   of memory formation. Therefore, therapeutic modulation of this gene or its protein product may be beneficial in the treatment of one or more of these diseases, as may stimulation and/or blockade of the receptor coded for by the gene.

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

5   1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures,

10   such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine

15   A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional

20   experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered

25   its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

30   2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per

5   action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response.

10 The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at

15 alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

20 3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic

25 receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to

30 increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA

receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, p < 0.05). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, p < 0.05). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 1.3D Summary: Ag2341 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag2341 Expression of the GMAC009642_C gene is highest in a sample derived from a sample of baldder cancer (CT = 34.5). In addition, there is substantial expression of this gene in a gastric cancer, two breast cancers, an ovarian cancer, a colon cancer, normal uterus, and a sample derived from normal colon tissue. Thus, the expression of this gene could be used to distinguish these tissue samples from others in the panel. Moreover, therapeutic modulation of this gene or its protein product, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of colon cancer, breast cancer, bladder cancer or ovarian cancer.

Panel 4D Summary: Ag2341 Low but significant expression of the GMAC009642_C gene is detected in a liver cirrhosis sample (CT = 33.08). This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for

the diagnosis of liver cirrhosis. Low level expression of this transcript was also detected in resting monocytes (CT=33.1) and normal lung (CT =34.7).

K. GMAC009758_A /CG148998-01: Olfactory Receptor

Expression of gene GMAC009758_A (also known as CG148998-01) was assessed using the primer-probe set Ag2336, described in Table KA. Results of the RTQ-PCR runs are shown in Tables KB and KC.

Table KA. Probe Name Ag2336

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tggctgaccttatcctgtctac-3'	22	225	252
Probe	TET-5'-actgtgcccaaggccctagccatatt-3'-TAMRA	26	251	253
Reverse	5'-atattgctccagcatagaacca-3'	22	278	254

Table KB. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag2336, Run 174461129	Tissue Name	Rel. Exp.(%) Ag2336, Run 174461129
Normal Colon	0.0	Kidney Margin (OD04348)	100.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	15.3
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0

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Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	15.1
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer	14.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	16.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	29.9	Normal Breast	16.8
Ovarian Margin (OD06283-07)	12.3	Breast Cancer	8.5
Ovarian Cancer	27.2	Breast Cancer	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	15.9	Breast Cancer Metastasis	0.0
Ovarian Margin (OD06455-07)	9.0	Breast Cancer	16.4
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	8.5
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	16.7
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	38.4
Lung Margin (OD05014B)	17.1	Normal Liver	12.9
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0

Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	15.6	Liver Tissue 6004-N	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0
Liver Margin (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer	0.0
Lung Margin (OD04321)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	45.4	Gastric Cancer 9060395	34.4
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table KC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2336, Run 164023173	Tissue Name	Rel. Exp.(%) Ag2336, Run 164023173
Secondary Th1 act	14.8	HUVEC IL-1beta	0.0
Secondary Th2 act	27.9	HUVEC IFN gamma	14.6
Secondary Tr1 act	7.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	24.8	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	14.2	HUVEC IL-11	0.0
Secondary Tr1 rest	19.8	Lung Microvascular EC none	0.0
Primary Th1 act	5.9	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	7.4	Microvascular Dermal EC none	6.3

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Primary Tr1 act	14.7	Microsvasular Dermal EC TNFalpha + IL-1beta	3.4
Primary Th1 rest	29.5	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	23.0	Small airway epithelium none	0.0
Primary Tr1 rest	11.6	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	6.5	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	9.9	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	15.6	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	4.7	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	7.4
2ry Th1/Th2/Tr1_anti-CD95 CH11	9.9	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	18.6	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	7.9
LAK cells IL-2	35.1	Liver cirrhosis	56.3
LAK cells IL-2+IL-12	33.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	**100.0**	NCI-H292 none	18.4
LAK cells IL-2+ IL-18	34.9	NCI-H292 IL-4	7.3
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	6.9
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	60.3	NCI-H292 IFN gamma	17.8
Two Way MLR 5 day	7.8	HPAEC none	0.0
Two Way MLR 7 day	24.7	HPAEC TNF alpha + IL-1 beta	6.9
PBMC rest	0.0	Lung fibroblast none	7.9
PBMC PWM	59.5	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	46.0	Lung fibroblast IFN	55.1

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		gamma	
B lymphocytes CD40L and IL-4	9.1	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	16.3
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	8.2	Dermal fibroblast IFN gamma	32.8
Dendritic cells LPS	3.1	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	6.8	IBD Crohn's	14.8
Monocytes LPS	14.7	Colon	7.4
Macrophages rest	9.2	Lung	8.5
Macrophages LPS	10.5	Thymus	26.6
HUVEC none	0.0	Kidney	21.8
HUVEC starved	7.1		

CNS_neurodegeneration_v1.0 Summary: Ag2336 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag2336 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5   **Panel 2.2 Summary:** Ag2336 Expression of this gene is low but significant in a sample of normal kidney (CT = 34.6). Therefore, expression of this gene could be used to distinguish kidney from other samples.

Panel 4D Summary: Ag2336 The GMAC009758_A gene is most highly expressed in LAK cells treated with IL-2 and IFN-gamma (CT = 33.3). It is also expressed at low levels in a
10   number of cell types of significance in the immune response, including B lymphocytes and peripheral blood mononuclear cells, as well as in tissue cells (normal and stimulated) such as lung fibroblasts. In general, expression of this gene appears to be up-regulated in response to interferon gamma treatment. Therefore, modulation of the activity of the protein product of this gene with a small molecule or antibody therapeutic may lead to altered functions of these
15   cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus

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erythematosus, or arthritis. Expression of this gene is also seen at low levels in liver cirrhosis suggests that antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

5

L. GMAL358773_A: GPCR

Expression of gene GMAL358773_A was assessed using the primer-probe sets Ag2335 and Ag2276, described in Tables LA and LB. Results of the RTQ-PCR runs are shown in Table LC.

10 Table LA. Probe Name Ag2335

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-aagaagatcccttccacagaag-3'	22	685	255
Probe	TET-5'-tatttgccttccacacttgctggttg-3'-TAMRA	26	726	256
Reverse	5'-caatgaatccagtggaaagaaa-3'	22	757	257

Table LB. Probe Name Ag2276

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-aagaagatcccttccacagaag-3'	22	685	258
Probe	TET-5'-tatttgccttccacacttgctggttg-3'-TAMRA	26	726	259
Reverse	5'-caatgaatccagtggaaagaaa-3'	22	757	260

Table LC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2335, Run 164021791	Rel. Exp.(%) Ag2335, Run 164022932	Tissue Name	Rel. Exp.(%) Ag2335, Run 164021791	Rel. Exp.(%) Ag2335, Run 164022932
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	22.7	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	0.0	0.0
Secondary Tr1 act	0.0	0.0	HUVEC TNF alpha + IFN	0.0	0.0

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		gamma		
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	6.4	Lung Microvascular EC none	0.0	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0
Primary Th1 rest	0.0	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	8.2	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0	0.0
CD45RA CD4 lymphocyte act	0.0	**100.0**	Coronery artery SMC rest	16.8	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8 lymphocyte rest	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0
Secondary CD8 lymphocyte act	0.0	0.0	KU-812 (Basophil) rest	23.3	13.4
CD4 lymphocyte none	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	**100.0**	49.3
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0

LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	0.0	0.0	Liver cirrhosis	42.9	22.7
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	0.0	0.0
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+IL-18	0.0	0.0	NCI-H292 IL-4	0.0	0.0
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	0.0	0.0
NK Cells IL-2 rest	0.0	0.0	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	0.0	NCI-H292 IFN gamma	0.0	0.0
Two Way MLR 5 day	5.6	0.0	HPAEC none	0.0	0.0
Two Way MLR 7 day	0.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	0.0
PBMC rest	0.0	0.0	Lung fibroblast none	0.0	0.0
PBMC PWM	0.0	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	0.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes CD40L and IL-4	0.0	0.0	Dermal fibroblast CCD1070 rest	0.0	16.8
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0
Dendritic cells none	0.0	0.0	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	8.7	0.0	Dermal fibroblast	0.0	0.0

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			IL-4		
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	0.0	0.0
Monocytes rest	0.0	0.0	IBD Crohn's	0.0	0.0
Monocytes LPS	0.0	0.0	Colon	7.3	0.0
Macrophages rest	4.6	3.9	Lung	9.2	4.5
Macrophages LPS	0.0	0.0	Thymus	0.0	0.0
HUVEC none	0.0	0.0	Kidney	0.0	0.0
HUVEC starved	0.0	0.0			

CNS_neurodegeneration_v1.0 Summary: Ag2335 Expression is of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag2276 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag2276/Ag2335 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag2235 Results from two experiments using the same probe/primer set showed some differences; only those results that were common to the two experiments are discussed here. The GMAL358773_A gene is expressed at low levels in the PMA and ionomycin treated basophil cell line KU-812 and to a lesser extent in untreated KU-812 cells. This gene encodes a putative GPCR and it is known that GPCR-type receptors are important in multiple physiological responses mediated by basophils. Therefore, antibody or small molecule therapies designed with the protein encoded for by this gene could block or inhibit inflammation or tissue damage due to basophil activation in response to asthma, allergies, hypersensitivity reactions, psoriasis, and viral infections. Ag2276 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

References:

1. Heinemann A., Hartnell A., Stubbs V.E., Murakami K., Soler D., LaRosa G., Askenase P.W., Williams T.J., Sabroe I. (2000) Basophil responses to chemokines are regulated by both sequential and cooperative receptor signaling. J. Immunol. 165: 7224-7233.

To investigate human basophil responses to chemokines, we have developed a sensitive assay that uses flow cytometry to measure leukocyte shape change as a marker of cell

responsiveness. PBMC were isolated from the blood of volunteers. Basophils were identified as a single population of cells that stained positive for IL-3Ralpha (CDw123) and negative for HLA-DR, and their increase in forward scatter (as a result of cell shape change) in response to chemokines was measured. Shape change responses of basophils to chemokines were highly reproducible, with a rank order of potency: monocyte chemoattractant protein (MCP) 4 (peak at <1 nM) >/= eotaxin-2 = eotaxin-3 >/= eotaxin > MCP-1 = MCP-3 > macrophage-inflammatory protein-1alpha > RANTES = MCP-2 = IL-8. The CCR4-selective ligand macrophage-derived chemokine did not elicit a response at concentrations up to 10 nM. Blocking mAbs to CCR2 and CCR3 demonstrated that responses to higher concentrations (>10 nM) of MCP-1 were mediated by CCR3 rather than CCR2, whereas MCP-4 exhibited a biphasic response consistent with sequential activation of CCR3 at lower concentrations and CCR2 at 10 nM MCP-4 and above. In contrast, responses to MCP-3 were blocked only in the presence of both mAbs, but not after pretreatment with either anti-CCR2 or anti-CCR3 mAb alone. These patterns of receptor usage were different from those seen for eosinophils and monocytes. We suggest that cooperation between CCRs might be a mechanism for preferential recruitment of basophils, as occurs in tissue hypersensitivity responses in vivo.

PMID: 11120855

M. GMAP002512_G/CG149038-01: Olfactory Receptor

Expression of gene GMAP002512_G (also known as CG149038-01) was assessed using the primer-probe set Ag2333, described in Table MA. Results of the RTQ-PCR runs are shown in Tables MB and MC.

Table MA. Probe Name Ag2333

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-agtcctcagcttcacacagcta-3'	22	187	261
Probe	TET-5'-ttttctcagccacgtagcttttgttt-3'-TAMRA	26	216	262
Reverse	5'-aggggtgatagaggaggtgtag-3'	22	249	263

Table MB. Panel 2.2

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Tissue Name	Rel. Exp.(%) Ag2333, Run 174461128	Tissue Name	Rel. Exp.(%) Ag2333, Run 174461128
Normal Colon	0.0	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	100.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	0.0
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer	0.1
Ovarian Cancer	0.6	Breast Cancer	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin	0.0	Breast Cancer Mets	0.0

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(OD06145)		(OD04590-03)	
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	0.0
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	0.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0
Liver Margin (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.2	Liver Cancer	0.0
Lung Margin (OD04321)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer	0.0
Kidney Margin (OD04338)	0.2	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin	0.0	Stomach Margin	0.0

(OD04340)		9060394	
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table MC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2333, Run 163945353	Tissue Name	Rel. Exp.(%) Ag2333, Run 163945353
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	19.1	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	2.2	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0

LAK cells IL-2	0.0	Liver cirrhosis	100.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	40.1	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	24.1
Monocytes rest	0.0	IBD Crohn's	44.1
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag2333 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

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Panel 1.3D Summary: Ag2333 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag2333 Expression of the GMAP002512_G gene is highest in a sample derived from normal kidney tissue adjacent to malignant kidney (CT = 26.5). Thus, the expression of this gene could be used to distinguish this sample of kidney tissue from the other samples in the panel.

Panel 4D Summary: Ag2333 Significant expression of the GMAP002512_G gene is detected only in liver cirrhosis (CT = 34.2). Furthermore, this transcript is not detected in normal liver in Panel 1.3D, suggesting that expression of this gene is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

N. GMAP002512_A/CG149158-01: Olfactory Receptor

Expression of gene GMAP002512_A (also known as CG149158-01) was assessed using the primer-probe sets Ag2326 and Ag1801, described in Tables NA and NB. Results of the RTQ-PCR runs are shown in Tables NC and ND.

Table NA. Probe Name Ag2326

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cgttatcactttccgtctgact-3'	22	485	264
Probe	TET-5'-ccatttctattgtgatgacctcccct-3'-TAMRA	26	530	265
Reverse	5'-gtctgagcaggacagagctaag-3'	22	557	266

Table NB. Probe Name Ag1801

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tgctggctttgatatgatctct-3'	22	611	267
Probe	TET-5'-cctcttccattgtcctcacctcctaca-3'-TAMRA	27	634	268
Reverse	5'-tagagcggatccttaggatagc-3'	22	675	269

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Table NC. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag2326, Run 174461118	Tissue Name	Rel. Exp.(%) Ag2326, Run 174461118
Normal Colon	0.0	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	24.1
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	0.0
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	**100.0**
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	0.0
Ovarian Margin (OD06283-07)	15.1	Breast Cancer	0.0
Ovarian Cancer	18.3	Breast Cancer	0.0
Ovarian cancer	0.0	Breast Cancer	0.0

(OD06145)		(OD04590-01)	
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	0.0
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	0.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0
Liver Margin (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer	0.0
Lung Margin (OD04321)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell	0.0	Gastric Cancer	11.4

type (OD04340)		9060395	
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table ND. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1801, Run 165810636	Rel. Exp.(%) Ag2326, Run 163945308	Tissue Name	Rel. Exp.(%) Ag1801, Run 165810636	Rel. Exp.(%) Ag2326, Run 163945308
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	5.3	0.0	HUVEC IFN gamma	0.0	0.0
Secondary Tr1 act	0.0	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	5.1	0.0
Primary Tr1 act	0.0	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0
Primary Th1 rest	0.0	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	0.0	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0	0.0

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CD45RA CD4 lymphocyte act	0.0	33.2	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8 lymphocyte rest	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0
Secondary CD8 lymphocyte act	0.0	0.0	KU-812 (Basophil) rest	0.0	0.0
CD4 lymphocyte none	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	0.0	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	0.0	0.0	Liver cirrhosis	**100.0**	**100.0**
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	0.0	0.0
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+IL-18	0.0	0.0	NCI-H292 IL-4	0.0	0.0
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	0.0	0.0
NK Cells IL-2 rest	0.0	0.0	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	0.0	NCI-H292 IFN gamma	0.0	0.0
Two Way MLR 5 day	0.0	0.0	HPAEC none	0.0	0.0
Two Way MLR 7 day	0.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	0.0
PBMC rest	0.0	0.0	Lung fibroblast none	0.0	0.0
PBMC PWM	0.0	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	0.0

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Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes CD40L and IL-4	0.0	0.0	Dermal fibroblast CCD1070 rest	0.0	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	5.3	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0
Dendritic cells none	0.0	0.0	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.0	32.3
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	22.8	38.4
Monocytes rest	0.0	0.0	IBD Crohn's	15.1	27.9
Monocytes LPS	0.0	0.0	Colon	0.0	0.0
Macrophages rest	0.0	0.0	Lung	0.0	0.0
Macrophages LPS	0.0	0.0	Thymus	0.0	0.0
HUVEC none	0.0	0.0	Kidney	0.0	0.0
HUVEC starved	0.0	0.0			

CNS_neurodegeneration_v1.0 Summary: Ag2326 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag1801/Ag2326 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag2326 Low but significant expression of the GMAP002512_A gene is detected in a thyroid cancer sample (CT = 34). Interestingly, the expression in the thyroid cancer sample is significantly higher than in the matched adjacent tissue. Thus, expression of this gene may be used as a marker to detect thyroid tumors. In addition, therapeutic modulation of the activity of this gene product, using small molecule drugs, antibodies or protein therapeutics, may be beneficial in the treatment of thyroid cancer. Ag1801 Expression

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of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag1801/Ag2326</u> Results from two experiments using different probe/primer sets are in good agreement. Low but significant expression of the GMAP002512_A gene is detected in a liver cirrhosis sample. Furthermore, this gene is not expressed in normal liver on Panel 1.3D, suggesting that expression of this gene is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

O. GMAC073647_A: GPCR

Expression of gene GMAC073647_A was assessed using the primer-probe set Ag1509, described in Table OA. Results of the RTQ-PCR runs are shown in Table OB.

<u>Table OA</u>. Probe Name Ag1509

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-aattgctcaaactatcctgcaa-3'	22	554	270
Probe	TET-5'-tcacggagtttatcctcttcttaatggctg-3'-TAMRA	30	587	271
Reverse	5'-agggatcaaagaaccaaagaga-3'	22	624	272

<u>Table OB</u>. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1509, Run 141961835	Tissue Name	Rel. Exp.(%) Ag1509, Run 141961835
Endothelial cells	0.0	Renal ca. 786-0	1.5
Heart (Fetal)	1.3	Renal ca. A498	5.1
Pancreas	0.5	Renal ca. RXF 393	0.0
Pancreatic ca. CAPAN 2	0.2	Renal ca. ACHN	2.5
Adrenal Gland	4.9	Renal ca. UO-31	3.8
Thyroid	0.5	Renal ca. TK-10	58.6
Salivary gland	13.7	Liver	5.9
Pituitary gland	0.5	Liver (fetal)	3.3

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Brain (fetal)	2.5	Liver ca. (hepatoblast) HepG2	16.8
Brain (whole)	2.2	Lung	0.0
Brain (amygdala)	5.9	Lung (fetal)	1.0
Brain (cerebellum)	3.2	Lung ca. (small cell) LX-1	11.0
Brain (hippocampus)	20.4	Lung ca. (small cell) NCI-H69	35.4
Brain (thalamus)	5.1	Lung ca. (s.cell var.) SHP-77	2.5
Cerebral Cortex	17.7	Lung ca. (large cell)NCI-H460	7.5
Spinal cord	0.7	Lung ca. (non-sm. cell) A549	5.7
Glio/astro U87-MG	0.6	Lung ca. (non-s.cell) NCI-H23	61.1
Glio/astro U-118-MG	2.3	Lung ca. (non-s.cell) HOP-62	18.2
astrocytoma SW1783	1.3	Lung ca. (non-s.cl) NCI-H522	0.0
Neuro*; met SK-N-AS	0.0	Lung ca. (squam.) SW 900	6.9
astrocytoma SF-539	0.7	Lung ca. (squam.) NCI-H596	11.4
astrocytoma SNB-75	2.3	Mammary gland	4.8
Glioma SNB-19	37.1	Breast ca.* (pl.ef) MCF-7	18.3
Glioma U251	1.1	Breast ca.* (pl.ef) MDA-MB-231	0.7
Glioma SF-295	0.2	Breast ca.* (pl. ef) T47D	4.0
Heart	11.8	Breast ca. BT-549	4.1
Skeletal Muscle	4.9	Breast ca. MDA-N	11.5
Bone marrow	6.5	Ovary	0.0
Thymus	0.5	Ovarian ca. OVCAR-3	0.7
Spleen	0.5	Ovarian ca. OVCAR-4	43.8
Lymph node	0.0	Ovarian ca. OVCAR-5	27.0
Colorectal	2.0	Ovarian ca. OVCAR-8	34.6
Stomach	0.5	Ovarian ca. IGROV-1	20.3

Small intestine	7.3	Ovarian ca. (ascites) SK-OV-3	24.8
Colon ca. SW480	0.6	Uterus	3.1
Colon ca.* SW620 (SW480 met)	0.3	Placenta	1.2
Colon ca. HT29	4.1	Prostate	18.6
Colon ca. HCT-116	13.6	Prostate ca.* (bone met) PC-3	0.5
Colon ca. CaCo-2	0.5	Testis	6.8
CC Well to Mod Diff (ODO3866)	8.0	Melanoma Hs688(A).T	0.0
Colon ca. HCC-2998	10.2	Melanoma* (met) Hs688(B).T	6.2
Gastric ca. (liver met) NCI-N87	9.1	Melanoma UACC-62	0.0
Bladder	23.8	Melanoma M14	33.7
Trachea	0.4	Melanoma LOX IMVI	1.2
Kidney	100.0	Melanoma* (met) SK-MEL-5	1.8
Kidney (fetal)	16.5		

Panel 1.2 Summary: Ag1509 Highest expression of the GMAC073647_A gene is seen in the normal kidney (CT=30.1). Overall, however, this gene appears to show a higher association in cell lines derived from cancers than in normal tissues. There is significant expression in a cluster of cell lines derived form ovarian, lung and colon cancers. Thus,

5   expression of this gene could be used to differentiate between these samples and other samples on this panel. Furthermore, expression of this gene could potentially be used as a marker for ovarian, colon or lung cancers.

Among tissues with metabolic function, this gene is expressed at low but significant levels in the heart (CT=33.2). Furthermore, this gene is expressed at higher levels in the adult

10   heart when compared to expression in the fetal heart (CT=36.4). Thus, expression of this gene could also be used to differentiate between adult and fetal source of this tissue.

This gene represents a novel G-protein coupled receptor (GPCR) with expression in the brain, including the amygdala, hippocampus, thalamus and cerebral cortex. The GPCR family of receptors contains a large number of neurotransmitter receptors, including the

15   dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and

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metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and a2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The b-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the a-adrenergic receptors have been implicated in memory. Therefore this gene may be of use as a small molecule target for the treatment of any of the described diseases.

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced

the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered

5   its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

10   2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which,

15   respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback

20   inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response. The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE

25   neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine

30   compared with the SSRIs.

3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the

5   strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis.

10   NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

15   4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9 Related Articles, Books, LinkOut

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261,

20   we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, p < 0.05). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive

25   rats (28% infarct volume reduction vs controls, p < 0.05). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

P. GMAC027522_A AND GMAC036216_C: GPCR

30   Expression of gene GMAC027522_A and variant GMAC036216_C was assessed using the primer-probe sets Ag2377, Ag2607, Ag2610, Ag1501 and Ag1585, described in

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Tables PA, PB, PC, PD and PE. Results of the RTQ-PCR runs are shown in Tables PF, PG, PH, PI, PJ, PK and PL.

Table PA. Probe Name Ag2377

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atgggaaacaccatcatcatag-3'	22	200	273
Probe	TET-5'-tggtcatagctgacacccacctacat-3'-TAMRA	26	225	274
Reverse	5'-aattgcccaggaagaagtacat-3'	22	257	275

Table PB. Probe Name Ag2607

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-catagctgacacccacctacat-3'	22	229	276
Probe	TET-5'-cacccatgtacttcttcctgggcaat-3'-TAMRA	26	252	277
Reverse	5'-actgcagtcatggttaccaaga-3'	22	294	278

5   Table PC. Probe Name Ag2610

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gtctcacctcacactggtcttc-3'	22	808	279
Probe	TET-5'-catctttctgtatgtcaggcctggca-3'-TAMRA	26	847	280
Reverse	5'-ctgacttgcacagagtgagctt-3'	22	873	281

Table PD. Probe Name Ag1501

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-catagctgacacccacctacat-3'	22	229	282
Probe	TET-5'-cacccatgtacttcttcctgggcaat-3'-TAMRA	26	252	283
Reverse	5'-ctgcagtcatggttaccaagat-3'	22	293	284

Table PE. Probe Name Ag1585

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-catagctgacacccacctacat-3'	22	229	285
Probe	TET-5'-cacccatgtacttcttcctgggcaat-3'-	26	252	286

	TAMRA						
Reverse	5'-ctgcagtcatggttaccaagat-3'			22	293	287	

Table PF. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2377, Run 208271229	Rel. Exp.(%) Ag2607, Run 208971580	Rel. Exp.(%) Ag2610, Run 208393679	Tissue Name	Rel. Exp.(%) Ag2377, Run 208271229	Rel. Exp.(%) Ag2607, Run 208971580	Rel. Exp.(%) Ag2610, Run 208393679
AD 1 Hippo	9.2	4.5	14.9	Control (Path) 3 Temporal Ctx	1.4	1.4	0.0
AD 2 Hippo	10.7	15.1	45.7	Control (Path) 4 Temporal Ctx	18.2	35.1	36.9
AD 3 Hippo	8.8	8.5	18.7	AD 1 Occipital Ctx	16.3	35.6	17.7
AD 4 Hippo	7.2	9.0	4.8	AD 2 Occipital Ctx (Missing)	0.0	0.0	0.0
AD 5 Hippo	32.5	44.4	48.0	AD 3 Occipital Ctx	10.3	13.0	18.9
AD 6 Hippo	**100.0**	35.6	33.9	AD 4 Occipital Ctx	16.4	57.4	20.0
Control 2 Hippo	24.0	33.4	22.5	AD 5 Occipital Ctx	11.8	27.5	22.4
Control 4 Hippo	5.6	7.4	13.9	AD 5 Occipital Ctx	3.6	18.0	13.6
Control (Path) 3 Hippo	4.0	6.2	0.0	Control 1 Occipital Ctx	7.2	7.7	2.6
AD 1 Temporal Ctx	36.6	60.3	27.4	Control 2 Occipital Ctx	0.1	55.5	25.3
AD 2 Temporal Ctx	18.3	39.5	46.3	Control 3 Occipital Ctx	19.3	29.1	32.3

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AD 3 Temporal Ctx	10.1	10.3	18.9	Control 4 Occipital Ctx	10.0	20.9	8.2
AD 4 Temporal Ctx	30.4	52.5	31.9	Control (Path) 1 Occipital Ctx	62.9	**100.0**	**100.0**
AD 5 Inf Temporal Ctx	35.1	85.3	52.5	Control (Path) 2 Occipital Ctx	23.5	47.6	12.9
AD 5 Sup Temporal Ctx	10.7	36.6	28.7	Control (Path) 3 Occipital Ctx	1.1	2.2	5.2
AD 6 Inf Temporal Ctx	27.5	87.7	60.7	Control (Path) 4 Occipital Ctx	30.8	46.0	39.2
AD 6 Sup Temporal Ctx	22.4	72.2	52.5	Control 1 Parietal Ctx	14.3	35.1	10.0
Control 1 Temporal Ctx	3.9	15.6	6.0	Control 2 Parietal Ctx	17.4	61.1	30.6
Control 2 Temporal Ctx	7.6	11.6	13.0	Control 3 Parietal Ctx	15.5	26.2	25.7
Control 3 Temporal Ctx	9.7	12.6	4.4	Control (Path) 1 Parietal Ctx	27.2	60.3	64.6
Control 3 Temporal Ctx	11.5	15.4	6.8	Control (Path) 2 Parietal Ctx	57.0	54.7	43.8
Control (Path) 1 Temporal Ctx	43.8	67.4	36.3	Control (Path) 3 Parietal Ctx	2.0	0.0	7.3
Control (Path) 2 Temporal Ctx	17.8	35.6	22.4	Control (Path) 4 Parietal Ctx	48.3	65.5	82.9

Table PG. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1501, Run 140466099	Tissue Name	Rel. Exp.(%) Ag1501, Run 140466099
Endothelial cells	6.8	Renal ca. 786-0	14.3
Heart (Fetal)	0.3	Renal ca. A498	12.6
Pancreas	0.6	Renal ca. RXF 393	15.9
Pancreatic ca. CAPAN 2	0.3	Renal ca. ACHN	11.8
Adrenal Gland	16.4	Renal ca. UO-31	21.0
Thyroid	0.0	Renal ca. TK-10	28.3
Salivary gland	38.2	Liver	7.6
Pituitary gland	1.2	Liver (fetal)	5.1
Brain (fetal)	20.6	Liver ca. (hepatoblast) HepG2	9.9
Brain (whole)	13.3	Lung	0.0
Brain (amygdala)	17.2	Lung (fetal)	0.9
Brain (cerebellum)	7.0	Lung ca. (small cell) LX-1	33.9
Brain (hippocampus)	67.4	Lung ca. (small cell) NCI-H69	58.6
Brain (thalamus)	92.0	Lung ca. (s.cell var.) SHP-77	3.6
Cerebral Cortex	85.3	Lung ca. (large cell)NCI-H460	24.0
Spinal cord	25.0	Lung ca. (non-sm. cell) A549	30.8
Glio/astro U87-MG	17.0	Lung ca. (non-s.cell) NCI-H23	81.8
Glio/astro U-118-MG	5.5	Lung ca. (non-s.cell) HOP-62	24.3
astrocytoma SW1783	7.2	Lung ca. (non-s.cl) NCI-H522	59.0
Neuro*; met SK-N-AS	1.5	Lung ca. (squam.) SW 900	10.4
astrocytoma SF-539	2.4	Lung ca. (squam.) NCI-H596	25.7
astrocytoma SNB-75	14.2	Mammary gland	15.3
glioma SNB-19	23.5	Breast ca.* (pl.ef) MCF-7	2.1
glioma U251	6.9	Breast ca.* (pl.ef) MDA-MB-231	2.3
glioma SF-295	18.8	Breast ca.* (pl. ef)	88.9

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		T47D	
Heart	50.7	Breast ca. BT-549	6.1
Skeletal Muscle	13.2	Breast ca. MDA-N	74.7
Bone marrow	7.5	Ovary	0.7
Thymus	0.0	Ovarian ca. OVCAR-3	14.3
Spleen	4.6	Ovarian ca. OVCAR-4	40.3
Lymph node	2.9	Ovarian ca. OVCAR-5	72.7
Colorectal	9.3	Ovarian ca. OVCAR-8	**100.0**
Stomach	0.7	Ovarian ca. IGROV-1	56.3
Small intestine	6.5	Ovarian ca. (ascites) SK-OV-3	16.4
Colon ca. SW480	1.5	Uterus	9.5
Colon ca.* SW620 (SW480 met)	16.2	Placenta	39.0
Colon ca. HT29	14.7	Prostate	8.8
Colon ca. HCT-116	7.6	Prostate ca.* (bone met) PC-3	39.0
Colon ca. CaCo-2	9.4	Testis	14.0
CC Well to Mod Diff (ODO3866)	31.2	Melanoma Hs688(A).T	1.3
Colon ca. HCC-2998	10.3	Melanoma* (met) Hs688(B).T	10.6
Gastric ca. (liver met) NCI-N87	21.3	Melanoma UACC-62	48.6
Bladder	36.6	Melanoma M14	69.7
Trachea	0.0	Melanoma LOX IMVI	0.0
Kidney	35.8	Melanoma* (met) SK-MEL-5	9.7
Kidney (fetal)	14.9		

Table PH. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1585, Run 165529870	Rel. Exp.(%) Ag2377, Run 165631765	Rel. Exp.(%) Ag2607, Run 166219825	Rel. Exp.(%) Ag2610, Run 166162989
Liver adenocarcinoma	5.1	5.6	0.0	0.0

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Pancreas	0.0	0.0	0.0	0.0
Pancreatic ca. CAPAN 2	0.0	0.0	0.0	5.6
Adrenal gland	0.0	0.0	0.0	0.0
Thyroid	0.0	0.0	0.0	0.0
Salivary gland	11.0	4.5	7.0	0.0
Pituitary gland	0.0	0.0	7.7	28.9
Brain (fetal)	31.2	53.2	12.7	21.0
Brain (whole)	56.3	48.6	**100.0**	**100.0**
Brain (amygdala)	15.4	0.0	31.9	0.0
Brain (cerebellum)	10.0	19.6	0.0	25.2
Brain (hippocampus)	5.5	20.3	17.3	7.0
Brain (substantia nigra)	54.3	80.7	49.3	31.6
Brain (thalamus)	26.2	58.2	55.5	72.2
Cerebral Cortex	5.6	0.0	14.3	0.0
Spinal cord	**100.0**	**100.0**	98.6	38.7
Glio/astro U87-MG	13.0	0.0	0.0	0.0
glio/astro U-118-MG	4.2	7.2	0.0	0.0
astrocytoma SW1783	0.0	0.0	19.9	0.0
neuro*; met SK-N-AS	0.0	0.0	0.0	0.0
astrocytoma SF-539	12.3	6.5	0.0	5.4
astrocytoma SNB-75	0.0	0.0	0.0	3.9
glioma SNB-19	2.1	4.0	4.5	18.2
glioma U251	19.3	0.0	0.0	0.0
glioma SF-295	23.5	0.0	0.0	0.0
Heart (Fetal)	0.0	0.0	0.0	0.0
Heart	12.4	10.7	0.0	0.0
Skeletal muscle (Fetal)	0.0	0.0	0.0	0.0
Skeletal muscle	6.1	0.0	0.0	0.0
Bone marrow	0.0	0.0	0.0	0.0
Thymus	0.0	0.0	0.0	0.0
Spleen	0.0	0.0	0.0	0.0
Lymph node	6.7	0.0	0.0	0.0
Colorectal	10.7	4.9	0.0	0.0
Stomach	0.0	0.0	0.0	7.2

Small intestine	0.0	0.0	0.0	0.0
Colon ca. SW480	0.0	0.0	0.0	5.2
Colon ca.* SW620 (SW480 met)	6.8	0.0	6.8	8.5
Colon ca. HT29	0.0	0.0	0.0	0.0
Colon ca. HCT-116	5.9	0.0	0.0	0.0
Colon ca. CaCo-2	0.0	6.6	0.0	0.0
CC Well to Mod Diff (ODO3866)	0.0	0.0	0.0	0.0
Colon ca. HCC-2998	0.0	0.0	0.0	0.0
Gastric ca. (liver met) NCI-N87	0.0	6.7	0.0	8.0
Bladder	2.8	0.0	9.9	17.4
Trachea	0.0	6.4	0.0	0.0
Kidney	0.0	0.0	0.0	0.0
Kidney (fetal)	0.0	0.0	0.0	12.3
Renal ca. 786-0	0.0	3.4	0.0	0.0
Renal ca. A498	6.9	0.0	0.0	6.1
Renal ca. RXF 393	0.0	9.5	0.0	7.9
Renal ca. ACHN	0.0	0.0	3.1	6.4
Renal ca. UO-31	11.0	0.0	0.0	0.0
Renal ca. TK-10	4.9	0.0	0.0	0.0
Liver	8.0	0.0	0.0	0.0
Liver (fetal)	0.0	0.0	0.0	0.0
Liver ca. (hepatoblast) HepG2	0.0	0.0	0.0	0.0
Lung	11.0	0.0	0.0	0.0
Lung (fetal)	0.0	0.0	0.0	0.0
Lung ca. (small cell) LX-1	3.5	14.0	7.4	0.0
Lung ca. (small cell) NCI-H69	0.0	0.0	0.0	0.0
Lung ca. (s.cell var.) SHP-77	0.0	0.0	0.0	4.1
Lung ca. (large cell)NCI-H460	3.3	0.0	0.0	0.0
Lung ca. (non-sm. cell) A549	0.0	0.0	0.0	0.0
Lung ca. (non-s.cell) NCI-H23	5.3	14.4	8.2	5.6

Lung ca. (non-s.cell) HOP-62	0.0	0.0	0.0	0.0
Lung ca. (non-s.cl) NCI-H522	0.0	0.0	0.0	0.0
Lung ca. (squam.) SW 900	7.2	5.4	0.0	0.0
Lung ca. (squam.) NCI-H596	0.0	0.0	0.0	0.0
Mammary gland	0.0	0.0	7.7	0.0
Breast ca.* (pl.ef) MCF-7	4.7	0.0	0.0	0.0
Breast ca.* (pl.ef) MDA-MB-231	0.0	0.0	0.0	6.0
Breast ca.* (pl. ef) T47D	14.0	0.0	6.9	29.3
Breast ca. BT-549	0.0	0.0	0.0	0.0
Breast ca. MDA-N	5.2	12.6	18.0	0.0
Ovary	0.0	0.0	0.0	0.0
Ovarian ca. OVCAR-3	0.0	0.0	15.8	0.0
Ovarian ca. OVCAR-4	0.0	0.0	0.0	5.0
Ovarian ca. OVCAR-5	7.7	0.0	11.7	4.5
Ovarian ca. OVCAR-8	29.7	15.9	18.3	8.0
Ovarian ca. IGROV-1	17.6	0.0	0.0	0.0
Ovarian ca. (ascites) SK-OV-3	0.0	0.0	0.0	6.4
Uterus	0.0	9.5	6.1	0.0
Placenta	51.8	21.5	43.2	39.0
Prostate	0.0	14.6	0.0	0.0
Prostate ca.* (bone met) PC-3	0.0	0.0	6.0	0.0
Testis	17.4	14.8	18.6	10.5
Melanoma Hs688(A).T	0.0	0.0	0.0	0.0
Melanoma* (met) Hs688(B).T	0.0	0.0	0.0	0.0
Melanoma UACC-62	0.0	3.7	0.0	6.9
Melanoma M14	6.4	35.6	12.1	0.0

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Melanoma LOX IMVI	0.0	0.0	0.0	0.0
Melanoma* (met) SK-MEL-5	0.0	0.0	0.0	10.4
Adipose	0.0	0.0	0.0	0.0

Table PI. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag2377, Run 174553776	Rel. Exp.(%) Ag2607, Run 175128152	Rel. Exp.(%) Ag2610, Run 174929487	Tissue Name	Rel. Exp.(%) Ag2377, Run 174553776	Rel. Exp.(%) Ag2607, Run 175128152	Rel. Exp.(%) Ag2610, Run 174929487
Normal Colon	0.0	0.0	0.0	Kidney Margin (OD04348)	0.0	20.7	13.8
Colon cancer (OD06064)	15.3	0.0	0.0	Kidney malignant cancer (OD06204B)	24.1	21.8	0.0
Colon Margin (OD06064)	0.0	0.0	0.0	Kidney normal adjacent tissue (OD06204E)	0.0	0.0	0.0
Colon cancer (OD06159)	0.0	0.0	0.0	Kidney Cancer (OD04450-01)	0.0	9.5	0.0
Colon Margin (OD06159)	0.0	0.0	0.0	Kidney Margin (OD04450-03)	0.0	0.0	0.0
Colon cancer (OD06297-04)	0.0	0.0	0.0	Kidney Cancer 8120613	0.0	0.0	0.0
Colon Margin (OD06297-015)	0.0	0.0	0.0	Kidney Margin 8120614	0.0	0.0	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	0.0	0.0	Kidney Cancer 9010320	0.0	0.0	0.0
CC Margin (ODO3921)	0.0	0.0	0.0	Kidney Margin 9010321	0.0	0.0	0.0

Colon cancer metastasis (OD06104)	0.0	0.0	0.0	Kidney Cancer 8120607	0.0	0.0	0.0
Lung Margin (OD06104)	0.0	0.0	0.0	Kidney Margin 8120608	0.0	0.0	0.0
Colon mets to lung (OD04451-01)	27.9	0.0	0.0	Normal Uterus	35.6	17.8	0.0
Lung Margin (OD04451-02)	32.5	0.0	0.0	Uterine Cancer 064011	0.0	0.0	0.0
Normal Prostate	0.0	0.0	0.0	Normal Thyroid	0.0	0.0	0.0
Prostate Cancer (OD04410)	0.0	0.0	0.0	Thyroid Cancer	0.0	0.0	0.0
Prostate Margin (OD04410)	0.0	0.0	0.0	Thyroid Cancer A302152	0.0	0.0	0.0
Normal Ovary	0.0	0.0	0.0	Thyroid Margin A302153	0.0	0.0	0.0
Ovarian cancer (OD06283-03)	10.7	0.0	0.0	Normal Breast	15.0	8.7	12.3
Ovarian Margin (OD06283-07)	0.0	0.0	18.0	Breast Cancer	0.0	0.0	0.0
Ovarian Cancer	0.0	24.1	13.8	Breast Cancer	84.1	36.1	16.0
Ovarian cancer (OD06145)	0.0	0.0	0.0	Breast Cancer (OD04590-01)	0.0	0.0	0.0
Ovarian Margin (OD06145)	34.9	0.0	0.0	Breast Cancer Mets (OD04590-03)	22.5	0.0	0.0
Ovarian cancer (OD06455-03)	24.7	0.0	0.0	Breast Cancer Metastasis	0.0	0.0	38.4

Ovarian Margin (OD06455-07)	9.9	0.0	0.0	Breast Cancer	0.0	19.1	16.0
Normal Lung	0.0	9.2	0.0	Breast Cancer 9100266	**100.0**	**100.0**	85.3
Invasive poor diff. lung adeno (ODO4945-01	12.7	0.0	0.0	Breast Margin 9100265	9.9	0.0	25.7
Lung Margin (ODO4945-03)	0.0	18.3	0.0	Breast Cancer A209073	0.0	0.0	0.0
Lung Malignant Cancer (OD03126)	0.0	0.0	0.0	Breast Margin A2090734	14.6	0.0	20.3
Lung Margin (OD03126)	0.0	0.0	0.0	Breast cancer (OD06083)	75.8	9.9	**100.0**
Lung Cancer (OD05014A)	0.0	0.0	18.7	Breast cancer node metastasis (OD06083)	16.6	25.3	37.6
Lung Margin (OD05014B)	19.5	6.0	0.0	Normal Liver	0.0	0.0	0.0
Lung cancer (OD06081)	25.9	9.3	0.0	Liver Cancer 1026	0.0	0.0	0.0
Lung Margin (OD06081)	0.0	0.0	0.0	Liver Cancer 1025	33.4	6.7	0.0
Lung Cancer (OD04237-01)	0.0	0.0	0.0	Liver Cancer 6004-T	0.0	0.0	0.0
Lung Margin (OD04237-02)	0.0	11.0	0.0	Liver Tissue 6004-N	0.0	0.0	0.0
Ocular Mel Met to Liver (ODO4310)	13.6	0.0	0.0	Liver Cancer 6005-T	0.0	0.0	0.0
Liver Margin (ODO4310)	0.0	0.0	0.0	Liver Tissue 6005-N	0.0	9.7	0.0
Melanoma Metastasis	0.0	2.6	0.0	Liver Cancer	0.0	0.0	0.0

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Lung Margin (OD04321)	0.0	0.0	0.0	Normal Bladder	0.0	0.0	13.7
Normal Kidney	17.9	0.0	0.0	Bladder Cancer	0.0	0.0	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	0.0	21.5	Bladder Cancer	0.0	0.0	20.2
Kidney Margin (OD04338)	0.0	0.0	0.0	Normal Stomach	0.0	0.0	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	15.3	0.0	43.5	Gastric Cancer 9060397	0.0	0.0	0.0
Kidney Margin (OD04339)	0.0	0.0	0.0	Stomach Margin 9060396	0.0	7.6	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	0.0	0.0	Gastric Cancer 9060395	33.2	7.6	51.8
Kidney Margin (OD04340)	0.0	12.2	0.0	Stomach Margin 9060394	0.0	0.0	21.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	0.0	0.0	Gastric Cancer 064005	0.0	0.0	0.0

Table PJ. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1585, Run 165373550	Rel. Exp.(%) Ag2377, Run 164216614	Rel. Exp.(%) Ag2607, Run 164160833	Rel. Exp.(%) Ag2610, Run 164216616
Secondary Th1 act	0.0	27.4	14.3	8.6
Secondary Th2 act	0.0	36.3	0.0	11.0
Secondary Tr1 act	0.0	10.5	9.4	25.7
Secondary Th1 rest	0.0	0.0	0.0	0.0
Secondary Th2 rest	0.0	0.0	0.0	0.0
Secondary Tr1 rest	0.0	12.9	0.0	0.0
Primary Th1 act	0.0	0.0	0.0	0.0
Primary Th2 act	0.0	8.1	0.0	14.7
Primary Tr1 act	0.0	25.3	10.3	17.0

Primary Th1 rest	0.1	28.1	53.2	22.1
Primary Th2 rest	0.0	69.3	23.3	19.5
Primary Tr1 rest	0.1	13.3	15.1	12.3
CD45RA CD4 lymphocyte act	0.0	0.0	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	34.4	7.3	3.9
CD8 lymphocyte act	0.0	8.7	9.2	16.6
Secondary CD8 lymphocyte rest	**100.0**	31.0	13.1	0.0
Secondary CD8 lymphocyte act	0.0	12.2	10.8	14.0
CD4 lymphocyte none	0.0	0.0	0.0	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	25.9	14.6	10.7
LAK cells rest	0.0	28.5	33.2	28.3
LAK cells IL-2	0.0	0.0	9.9	0.0
LAK cells IL-2+IL-12	0.0	20.0	0.0	0.0
LAK cells IL-2+IFN gamma	0.0	12.2	10.0	0.0
LAK cells IL-2+ IL-18	0.0	9.4	0.0	0.0
LAK cells PMA/ionomycin	0.0	18.9	0.0	11.1
NK Cells IL-2 rest	0.0	25.5	17.4	15.5
Two Way MLR 3 day	0.0	31.2	5.4	0.0
Two Way MLR 5 day	0.0	0.0	12.0	8.8
Two Way MLR 7 day	0.0	10.6	0.0	0.0
PBMC rest	0.0	11.4	5.0	0.0
PBMC PWM	0.0	12.2	19.5	32.8
PBMC PHA-L	0.0	28.1	18.6	0.0
Ramos (B cell) none	0.0	13.9	18.8	0.0
Ramos (B cell) ionomycin	0.0	16.6	7.8	24.1
B lymphocytes PWM	0.0	15.7	12.9	10.5
B lymphocytes CD40L and IL-4	0.0	24.8	0.0	0.0
EOL-1 dbcAMP	0.0	13.7	7.4	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	6.2	0.0	0.0
Dendritic cells none	0.0	15.5	29.5	23.8
Dendritic cells LPS	0.0	10.7	17.0	0.0
Dendritic cells anti-	0.0	11.5	5.6	0.0

CD40				
Monocytes rest	0.0	0.0	0.0	8.0
Monocytes LPS	0.1	**100.0**	50.3	**100.0**
Macrophages rest	0.1	76.8	**100.0**	75.8
Macrophages LPS	0.0	8.0	8.5	0.0
HUVEC none	0.0	9.0	0.0	0.0
HUVEC starved	0.1	41.8	2.8	6.0
HUVEC IL-1beta	0.0	0.0	0.0	0.0
HUVEC IFN gamma	0.0	0.0	4.0	10.2
HUVEC TNF alpha + IFN gamma	0.0	0.0	4.0	0.0
HUVEC TNF alpha + IL4	0.0	12.4	6.7	0.0
HUVEC IL-11	0.0	12.6	0.0	0.0
Lung Microvascular EC none	0.0	18.7	16.7	6.8
Lung Microvascular EC TNFalpha + IL-1beta	0.1	0.0	12.9	23.3
Microvascular Dermal EC none	0.0	35.1	4.5	3.8
Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	8.2	10.7	15.8
Bronchial epithelium TNFalpha + IL1beta	0.0	0.0	0.0	7.1
Small airway epithelium none	0.0	0.0	0.0	0.0
Small airway epithelium TNFalpha + IL-1beta	0.0	0.0	10.7	5.9
Coronery artery SMC rest	0.0	12.2	0.0	0.0
Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0	0.0	0.0
Astrocytes rest	0.0	19.1	5.1	3.8
Astrocytes TNFalpha + IL-1beta	0.0	8.9	0.0	0.0
KU-812 (Basophil) rest	0.0	0.0	0.0	0.0
KU-812 (Basophil) PMA/ionomycin	0.0	13.9	5.6	0.0
CCD1106 (Keratinocytes) none	0.0	10.7	4.3	0.0
CCD1106	0.0	12.7	0.0	13.5

(Keratinocytes) TNFalpha + IL-1beta				
Liver cirrhosis	0.1	81.8	50.0	22.7
Lupus kidney	0.0	23.2	8.6	18.3
NCI-H292 none	0.0	0.0	3.7	20.4
NCI-H292 IL-4	0.0	44.4	0.0	7.2
NCI-H292 IL-9	0.0	7.0	0.0	0.0
NCI-H292 IL-13	0.0	0.0	3.9	0.0
NCI-H292 IFN gamma	0.0	11.0	1.9	11.0
HPAEC none	0.0	6.3	11.3	0.0
HPAEC TNF alpha + IL-1 beta	0.0	24.3	4.5	0.0
Lung fibroblast none	0.0	0.0	0.0	15.3
Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0	0.0	7.4
Lung fibroblast IL-4	0.0	0.0	0.0	9.7
Lung fibroblast IL-9	0.0	0.0	3.3	0.0
Lung fibroblast IL-13	5.1	0.0	0.0	0.0
Lung fibroblast IFN gamma	0.0	0.0	5.1	11.0
Dermal fibroblast CCD1070 rest	0.0	2.4	15.7	12.9
Dermal fibroblast CCD1070 TNF alpha	0.0	66.4	10.4	18.8
Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0	0.0	0.0
Dermal fibroblast IFN gamma	0.0	15.1	7.5	0.0
Dermal fibroblast IL-4	0.0	0.0	0.0	0.0
IBD Colitis 2	0.0	10.7	0.0	12.2
IBD Crohn's	0.0	0.0	0.0	6.1
Colon	0.0	0.0	0.0	9.0
Lung	0.0	0.0	4.5	14.5
Thymus	0.1	24.1	13.7	7.8
Kidney	0.0	44.4	17.7	19.6

Table PK. Panel CNS_1

Tissue Name	Rel. Exp.(%) Ag2377, Run 171656285	Rel. Exp.(%) Ag2377, Run 182012511	Tissue Name	Rel. Exp.(%) Ag2377, Run 171656285	Rel. Exp.(%) Ag2377, Run 182012511
BA4 Control	6.1	7.4	BA17 PSP	0.0	21.0

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BA4 Control2	8.8	4.2	BA17 PSP2	11.1	10.4
BA4 Alzheimer's2	0.0	7.1	Sub Nigra Control	42.3	41.2
BA4 Parkinson's	24.7	19.8	Sub Nigra Control2	29.5	3.6
BA4 Parkinson's2	17.8	30.8	Sub Nigra Alzheimer's2	28.5	12.6
BA4 Huntington's	17.6	3.7	Sub Nigra Parkinson's2	55.1	61.1
BA4 Huntington's2	8.1	0.0	Sub Nigra Huntington's	**100.0**	**100.0**
BA4 PSP	38.2	12.2	Sub Nigra Huntington's2	17.3	21.2
BA4 PSP2	20.0	5.2	Sub Nigra PSP2	9.7	5.4
BA4 Depression	49.7	31.2	Sub Nigra Depression	87.1	42.0
BA4 Depression2	14.2	18.0	Sub Nigra Depression2	33.0	20.4
BA7 Control	23.3	2.7	Glob Palladus Control	28.5	25.7
BA7 Control2	25.5	11.5	Glob Palladus Control2	25.2	15.2
BA7 Alzheimer's2	18.9	4.4	Glob Palladus Alzheimer's	11.9	16.4
BA7 Parkinson's	11.4	9.8	Glob Palladus Alzheimer's2	4.2	36.9
BA7 Parkinson's2	0.0	14.6	Glob Palladus Parkinson's	37.9	44.4
BA7 Huntington's	23.7	10.9	Glob Palladus Parkinson's2	9.0	26.1
BA7 Huntington's2	42.9	26.8	Glob Palladus PSP	48.0	33.4
BA7 PSP	30.8	14.6	Glob Palladus PSP2	10.7	9.9
BA7 PSP2	4.2	10.4	Glob Palladus Depression	40.9	39.5
BA7 Depression	31.9	21.3	Temp Pole Control	0.0	0.0
BA9 Control	2.0	4.4	Temp Pole Control2	11.8	7.9
BA9 Control2	16.7	24.7	Temp Pole Alzheimer's	0.0	0.0
BA9	0.0	6.6	Temp Pole	0.0	3.4

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Alzheimer's			Alzheimer's2		
BA9 Alzheimer's2	2.9	0.0	Temp Pole Parkinson's	17.3	7.1
BA9 Parkinson's	11.3	15.2	Temp Pole Parkinson's2	0.0	9.5
BA9 Parkinson's2	7.9	4.2	Temp Pole Huntington's	0.0	4.9
BA9 Huntington's	39.8	14.5	Temp Pole PSP	6.7	6.3
BA9 Huntington's2	8.1	3.7	Temp Pole PSP2	0.0	0.0
BA9 PSP	44.4	5.7	Temp Pole Depression2	0.0	23.8
BA9 PSP2	0.0	0.0	Cing Gyr Control	31.2	27.4
BA9 Depression	15.1	5.9	Cing Gyr Control2	16.8	24.5
BA9 Depression2	14.4	8.7	Cing Gyr Alzheimer's	17.8	13.2
BA17 Control	47.0	30.4	Cing Gyr Alzheimer's2	13.9	3.4
BA17 Control2	28.7	5.4	Cing Gyr Parkinson's	26.2	30.8
BA17 Alzheimer's2	7.5	7.1	Cing Gyr Parkinson's2	24.8	25.9
BA17 Parkinson's	38.2	68.3	Cing Gyr Huntington's	30.8	28.7
BA17 Parkinson's2	24.0	9.3	Cing Gyr Huntington's2	20.7	14.2
BA17 Huntington's	36.1	13.8	Cing Gyr PSP	90.1	76.3
BA17 Huntington's2	15.2	16.4	Cing Gyr PSP2	0.0	20.3
BA17 Depression	58.6	27.7	Cing Gyr Depression	52.5	61.1
BA17 Depression2	65.5	60.3	Cing Gyr Depression2	43.5	15.3

Table PL. Panel CNS_1.1

Tissue Name	Rel. Exp.(%) Ag2377, Run 200060897	Rel. Exp.(%) Ag2377, Run 200061715	Tissue Name	Rel. Exp.(%) Ag2377, Run 200060897	Rel. Exp.(%) Ag2377, Run 200061715
Cing Gyr	39.2	13.9	BA17 PSP2	5.3	11.8

Depression2					
Cing Gyr Depression	35.8	23.2	BA17 PSP	4.2	13.1
Cing Gyr PSP2	6.2	2.8	BA17 Huntington's2	17.8	10.1
Cing Gyr PSP	**100.0**	**100.0**	BA17 Huntington's	36.9	6.9
Cing Gyr Huntington's2	32.5	10.4	BA17 Parkinson's2	19.2	12.2
Cing Gyr Huntington's	27.4	8.8	BA17 Parkinson's	37.4	19.1
Cing Gyr Parkinson's2	12.8	1.9	BA17 Alzheimer's2	7.7	0.0
Cing Gyr Parkinson's	47.6	32.5	BA17 Control2	35.8	20.0
Cing Gyr Alzheimer's2	0.0	7.2	BA17 Control	35.1	22.7
Cing Gyr Alzheimer's	13.8	3.6	BA9 Depression2	8.6	3.8
Cing Gyr Control2	77.9	1.4	BA9 Depression	0.0	14.1
Cing Gyr Control	30.1	11.7	BA9 PSP2	3.6	12.4
Temp Pole Depression2	0.0	14.8	BA9 PSP	48.6	18.3
Temp Pole PSP2	0.0	4.5	BA9 Huntington's2	6.9	5.0
Temp Pole PSP	5.5	3.3	BA9 Huntington's	59.0	8.4
Temp Pole Huntington's	0.0	7.7	BA9 Parkinson's2	0.0	2.5
Temp Pole Parkinson's2	0.0	0.0	BA9 Parkinson's	7.9	0.0
Temp Pole Parkinson's	27.5	4.9	BA9 Alzheimer's2	0.0	0.0
Temp Pole Alzheimer's2	0.0	0.0	BA9 Alzheimer's	0.0	0.0
Temp Pole Alzheimer's	0.0	0.0	BA9 Control2	26.4	12.2
Temp Pole Control2	21.3	8.4	BA9 Control	15.1	0.0
Temp Pole Control	0.0	0.0	BA7 Depression	29.3	11.1
Glob Palladus	35.8	16.4	BA7 PSP2	28.7	2.9

Depression					
Glob Palladus PSP2	5.5	5.0	BA7 PSP	7.0	6.6
Glob Palladus PSP	23.7	8.6	BA7 Huntington's2	18.6	23.7
Glob Palladus Parkinson's2	34.2	6.5	BA7 Huntington's	11.3	6.7
Glob Palladus Parkinson's	16.4	20.3	BA7 Parkinson's2	0.0	0.0
Glob Palladus Alzheimer's2	19.5	3.4	BA7 Parkinson's	9.5	1.2
Glob Palladus Alzheimer's	24.3	6.7	BA7 Alzheimer's2	19.6	0.0
Glob Palladus Control2	13.8	2.8	BA7 Control2	25.3	2.4
Glob Palladus Control	33.2	17.7	BA7 Control	10.1	9.6
Sub Nigra Depression2	36.3	5.5	BA4 Depression2	27.5	15.9
Sub Nigra Depression	52.5	10.4	BA4 Depression	10.8	15.6
Sub Nigra PSP2	12.4	15.9	BA4 PSP2	15.2	17.0
Sub Nigra Huntington's2	8.7	5.9	BA4 PSP	11.3	10.7
Sub Nigra Huntington's	82.4	51.1	BA4 Huntington's2	0.0	0.0
Sub Nigra Parkinson's2	34.9	12.5	BA4 Huntington's	0.0	3.8
Sub Nigra Alzheimer's2	34.2	15.0	BA4 Parkinson's2	18.7	11.7
Sub Nigra Control2	6.3	5.3	BA4 Parkinson's	54.0	3.2
Sub Nigra Control	58.6	10.2	BA4 Alzheimer's2	6.2	0.0
BA17 Depression2	39.2	9.3	BA4 Control2	0.0	4.2
BA17 Depression	43.5	50.7	BA4 Control	35.6	4.7

CNS_neurodegeneration_v1.0 Summary: Ag2610/Ag2607/Ag2377 The GMAC027522_A gene is expressed more highly in the temporal cortex of Alzheimer's diseased brain than in control brain without amyloid plaques, which are diagnostic and potentially causative of

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Alzheimer's disease. The GMAC027522_A gene encodes a protein with homology to GPCRs. GPCRs are readily targetable with drugs, and regulate many specific brain processes, including signaling processes, that are currently the target of FDA-approved pharmaceuticals that treat Alzheimer's disease, such as the cholinergic system. The major mechanisms

5   proposed for AbetaP-induced cytotoxicity involve the loss of Ca2+ homeostasis and the generation of reactive oxygen species (ROS). The changes in Ca2+ homeostasis could be the result of changes in G-protein-driven releases of second messengers. Thus, targeting this class of molecule can have therapeutic potential in Alzheimer's disease treatment. In particular, the increased GMAC027522_A gene expression in brains affected by Alzheimer's

10   indicates potential therapeutic value to drugs that target this GPCR.

References:

1. Perrine K, Dogali M, Fazzini E, Sterio D, Kolodny E, Eidelberg D, Devinsky O, Beric A.Cognitive functioning after pallidotomy for refractory Parkinson's disease. J Neurol Neurosurg Psychiatry 1998 Aug;65(2):150-4.

15   BACKGROUND: Earlier approaches to pallidotomy for refractory Parkinson's disease had significant complication rates. More recent approaches show fewer complications, but the effect of pallidotomy on cognition is unclear. The current study was conducted to examine the neuropsychological effects of unilateral pallidotomy. METHODS: Neuropsychological testing was performed on patients with medically refractory, predominantly unilateral

20   Parkinson's disease at baseline and after unilateral ventral pallidotomy (n=28) or after an equivalent period without surgery in control patients (n=10). RESULTS: Pallidotomy patients showed no significant changes from baseline to retesting relative to the control group for any measure. Across all of the tests administered, only five of the surgery patients showed a significant decline, and of these five none declined on more than one test. Depression did not

25   relate to preoperative or postoperative cognition. The pallidotomy group showed a significant improvement in motor functioning and activities of daily living whereas the control group did not. These measures were not associated with the neuropsychological test scores at baseline or retest. CONCLUSIONS: Stereotactic unilateral ventral pallidotomy does not seem to produce dramatic cognitive declines in most patients.

30   PMID: 9703163

2. Kourie JI. Mechanisms of amyloid beta protein-induced modification in ion transport systems: implications for neurodegenerative diseases. Cell Mol Neurobiol 2001 Jun;21(3):173-213

1. Alzheimer's disease (AD) is a neurodegenerative disorder that affects the cognitive
5   function of the brain. Pathological changes in AD are characterized by the formation of amyloid plaques and neurofibrillary tangles as well as extensive neuronal loss. Abnormal proteolytic processing of amyloid precursor protein (APP) is the central step that leads to formation of amyloid plaque, neurofibrillary tangles, and neuronal loss. 2. The plaques, which accumulate extracellularly in the brain, are composed of aggregates and cause direct
10   neurotoxic effects and/or increase neuronal vulnerability to excitotoxic insults. The aggregates consist of soluble pathologic amyloid beta peptides AbetaP[1-42] and AbetaP[1-43] and soluble nonpathologic AbetaP[1-40]. Both APP and AbetaP interact with ion transport systems. AbetaP induces a wide range of effects as the result of activating a cascade of mechanisms. 3. The major mechanisms proposed for AbetaP-induced cytotoxicity involve
15   the loss of Ca2+ homeostasis and the generation of reactive oxygen species (ROS). The changes in Ca2+ homeostasis could be the result of (1) changes in endogenous ion transport systems, e.g. Ca2+ and K+ channels and Na+/K+-ATPase, and membrane receptor proteins, such as ligand-driven ion channels and G-protein-driven releases of second messengers, and (2) formation of heterogeneous ion channels. 4. The consequences of changes in Ca2+-
20   homeostasis-induced generation of ROS are (a) direct modification of intrinsic ion transport systems and their regulatory mechanisms, and (b) indirect effects on ion transport systems via peroxidation of phospholipids in the membrane, inhibition of phosphorylation, and reduction of ATP levels and cytoplasmic pH. 5. We propose that in AD, AbetaP with its different conformations alters cell regulation by modifying several ion transport systems and also by
25   forming heterogeneous ion channels. The changes in membrane transport systems are proposed as early steps in impairing neuronal function preceding plaque formation. We conclude that these changes damage the membrane by compromising its integrity and increasing its ion permeability. This mechanism of membrane damage is not only central for AD but also may explain other malfunctioned protein-processing-related pathologies.

30   PMID: 11569534

Panel 1.2 Summary: Ag1501 The GMAC027522_A gene is expressed at moderate levels throughout many of the samples in this panel. Highest expression is detected in an ovarian

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cancer cell line (CT=30.7). In addition, this gene is overexpressed in all six ovarian cancer cell lines present in this panel when compared to expression in normal ovary. The GMAC027522_A gene is also moderately expressed in cell lines derived from melanoma, breast cancer, and lung cancer. Thus, the expression of this gene could be used to distinguish

5 these cell lines from other tissue samples. In addition, therapeutic modulation of the GMAC027522_A gene or its protein product, through the use of small molecule drugs or antibodies, might be useful in the treatment of ovarian cancer, breast cancer, lung cancer or melanoma.

Among tissues involved in metabolic function, the GMAC027522_A gene is
10 moderately expressed in the adrenal gland, heart, skeletal muscle, and adult liver. Interestingly, GMAC027522_A gene expression is much lower in fetal liver and heart tissues than in the corresponding adult tissues. Thus, expression of the GMAC027522_A gene could be used to differentiate between adult and fetal tissues derived from the heart and liver. Furthermore, this gene or its protein product may be important in the pathogenesis and/or
15 treatment of disease in any or all of the above-named tissues.

There is widespread moderate expression of the GMAC027522_A gene across many of the samples derived from the CNS, including the amygdala, cerebellum, hippocampus, thalamus, cerebral cortex, and spinal cord. Please see CNS_neurodegeneration_panel_v1.0 summary for description of potential utility in the treatment of CNS disorders.

20 **Panel 1.3D Summary:** Ag2610/Ag2607/Ag1585/Ag2377 Expression of the GMAC027522_A gene appears to be limited to tissues involved in central nervous system function on this panel. Specifically, low but significant expression is detected in the thalamus, substantia nigra, spinal cord and fetal brain. Ag2545 Expression of the GMAC027522_A gene is low/undetectable (CT values >35) in all samples on this panel (data not shown).

25 **Panel 2.2 Summary:** Ag2377 Expression of the GMAC027522_A gene is highest in a sample derived from a breast cancer sample (CT = 34.7). Thus, the expression of this gene could be used to distinguish breast cancer samples from other samples and as a diagnostic marker for the presence of breast cancer. Furthermore, therapeutic modulation of the GMAC027522_A gene or the activity of its protein product, through the use of small
30 molecule drugs or antibodies, might be effective in the treatment of breast cancer.

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<u>Ag2610/Ag2607/Ag1585</u> Expression of the GMAC027522_A gene is low/undetectable (CT values >35) in all samples on this panel (data not shown).

Panel 4D Summary: <u>Ag2607/Ag1585/Ag2377</u> Experiments using three different probe/primer sets show disparate results and are uninterpretable (data not shown).

5   **Panel CNS_1 Summary:** <u>Ag2377</u> Two experiments with the same probe and primer set produce results that are in very good agreement. Expression of the GMAC027522_A gene is highest in the substantia nigra of a Huntington's disease patient, indicating that this gene may participate in the genetic dysregulation associated with the neurodegeneration that occurs in this brain region. The substantia nigra is also critical to the progression of Parkinson's disease

10   neurodegeneration. Thus, pharmacological targeting of the GPCR encoded by the GMAC027522_A gene may help counter this genetic dysregulation and contribute to the restoration of normal function in Huntington's disease as well as potentially Parkinson's disease patients. Pharmacological modulation of GPCR signaling systems is the mechanism by which powerful depression therapies, such as SSRIs, exert their effect.

15   **Panel CNS_1.1 Summary:** <u>Ag2377</u> In two experiments using the same probe and primer, highest expression is seen in the cingulate gyrus of patients with para supranuclear palsy PSP (CTs = 32) and depression. This observation indicates that targeting this GPCR could have therapeutic value in the treatment of these diseases.

20   **Q. GMAC036216_B: GPCR**

Expression of gene GMAC036216_B was assessed using the primer-probe sets Ag2606 and Ag1153, described in Tables QA and QB. Results of the RTQ-PCR runs are shown in Tables QC, QD, QE and QF.

<u>Table QA</u>. Probe Name Ag2606

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-acacacaggccaccaacttata-3'	22	588	288
Probe	TET-5'-ctttcactggccatctcaggtatgga-3'-TAMRA	26	620	289

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| Reverse | 5'-gtccataggagccagtgatacc-3' | 22 | 653 | 290 |

Table QB. Probe Name Ag1153

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-acacaggccaccaacttatatg-3'	22	590	291
Probe	TET-5'-ctttcactggccatctcaggtatgga-3'-TAMRA	26	620	292
Reverse	5'-gagtccataggagccagtgata-3'	22	655	293

Table QC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2606, Run 208393247	Tissue Name	Rel. Exp.(%) Ag2606, Run 208393247
AD 1 Hippo	15.3	Control (Path) 3 Temporal Ctx	3.5
AD 2 Hippo	22.5	Control (Path) 4 Temporal Ctx	33.9
AD 3 Hippo	3.1	AD 1 Occipital Ctx	10.1
AD 4 Hippo	8.7	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	43.5	AD 3 Occipital Ctx	8.0
AD 6 Hippo	45.1	AD 4 Occipital Ctx	9.1
Control 2 Hippo	17.9	AD 5 Occipital Ctx	16.2
Control 4 Hippo	10.2	AD 5 Occipital Ctx	17.2
Control (Path) 3 Hippo	2.2	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	16.0	Control 2 Occipital Ctx	21.9
AD 2 Temporal Ctx	8.7	Control 3 Occipital Ctx	15.9
AD 3 Temporal Ctx	12.4	Control 4 Occipital Ctx	1.7
AD 4 Temporal Ctx	7.5	Control (Path) 1 Occipital Ctx	54.7
AD 5 Inf Temporal Ctx	**100.0**	Control (Path) 2 Occipital Ctx	0.0
AD 5 Sup Temporal Ctx	16.3	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	52.1	Control (Path) 4 Occipital Ctx	3.2
AD 6 Sup Temporal Ctx	59.0	Control 1 Parietal Ctx	19.8

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Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	32.1
Control 2 Temporal Ctx	22.2	Control 3 Parietal Ctx	9.7
Control 3 Temporal Ctx	15.9	Control (Path) 1 Parietal Ctx	45.4
Control 3 Temporal Ctx	18.6	Control (Path) 2 Parietal Ctx	15.9
Control (Path) 1 Temporal Ctx	66.0	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	49.7	Control (Path) 4 Parietal Ctx	12.7

Table QD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2606, Run 166162876	Tissue Name	Rel. Exp.(%) Ag2606, Run 166162876
Liver adenocarcinoma	26.6	Kidney (fetal)	0.0
Pancreas	41.5	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	17.3	Renal ca. A498	36.6
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	16.0	Renal ca. ACHN	0.0
Salivary gland	18.4	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	29.7	Liver	0.0
Brain (whole)	38.2	Liver (fetal)	0.0
Brain (amygdala)	11.7	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	93.3	Lung	0.0
Brain (hippocampus)	79.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	76.8
Brain (thalamus)	11.8	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	35.6	Lung ca. (s.cell var.) SHP-77	12.9
Spinal cord	12.4	Lung ca. (large cell)NCI-H460	0.0
Glio/astro U87-MG	9.0	Lung ca. (non-sm. cell) A549	0.0
Glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0

astrocytoma SW1783	56.3	Lung ca. (non-s.cell) HOP-62	9.7
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	18.6
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	15.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	13.5	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	11.4	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	8.1
Spleen	0.0	Ovarian ca. OVCAR-5	49.7
Lymph node	15.6	Ovarian ca. OVCAR-8	0.0
Colorectal	34.4	Ovarian ca. IGROV-1	8.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	0.0
Small intestine	17.2	Uterus	8.7
Colon ca. SW480	0.0	Placenta	37.4
Colon ca.* SW620 (SW480 met)	**100.0**	Prostate	0.0
Colon ca. HT29	20.9	Prostate ca.* (bone met) PC-3	14.9
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	15.3	Melanoma UACC-62	16.3
Gastric ca. (liver met)	14.6	Melanoma M14	0.0

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NCI-N87				
Bladder	28.5	Melanoma LOX IMVI		0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5		0.0
Kidney	16.6	Adipose		0.0

Table QE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1153, Run 140011775	Rel. Exp.(%) Ag2606, Run 164204901	Tissue Name	Rel. Exp.(%) Ag1153, Run 140011775	Rel. Exp.(%) Ag2606, Run 164204901
Secondary Th1 act	0.0	6.7	HUVEC IL-1beta	0.0	4.9
Secondary Th2 act	12.8	3.7	HUVEC IFN gamma	20.3	28.7
Secondary Tr1 act	12.0	10.9	HUVEC TNF alpha + IFN gamma	7.4	7.1
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	7.6	27.2
Secondary Th2 rest	5.7	0.0	HUVEC IL-11	20.2	0.0
Secondary Tr1 rest	0.0	9.9	Lung Microvascular EC none	15.0	14.9
Primary Th1 act	6.0	6.7	Lung Microvascular EC TNFalpha + IL-1beta	16.7	8.8
Primary Th2 act	4.7	0.0	Microvascular Dermal EC none	26.2	5.6
Primary Tr1 act	0.0	13.6	Microsvasular Dermal EC TNFalpha + IL-1beta	38.7	4.7
Primary Th1 rest	29.1	5.5	Bronchial epithelium TNFalpha + IL1beta	21.3	6.9
Primary Th2 rest	29.5	5.8	Small airway epithelium none	16.0	3.1
Primary Tr1 rest	64.6	25.3	Small airway epithelium TNFalpha + IL-1beta	45.1	19.3
CD45RA CD4 lymphocyte act	7.3	4.6	Coronery artery SMC rest	9.9	13.9
CD45RO CD4 lymphocyte act	13.5	6.6	Coronery artery SMC TNFalpha + IL-1beta	0.0	23.8
CD8 lymphocyte	13.3	11.3	Astrocytes rest	4.5	11.1

act					
Secondary CD8 lymphocyte rest	14.3	10.4	Astrocytes TNFalpha + IL-1beta	31.0	72.7
Secondary CD8 lymphocyte act	0.0	6.7	KU-812 (Basophil) rest	40.9	12.5
CD4 lymphocyte none	6.8	9.0	KU-812 (Basophil) PMA/ionomycin	18.6	32.8
2ry Th1/Th2/Tr1_anti-CD95 CH11	27.0	22.2	CCD1106 (Keratinocytes) none	8.5	4.9
LAK cells rest	49.7	23.8	93580_CCD1106 (Keratinocytes)_TNFa and IFNg	32.5	
LAK cells IL-2	45.4	17.7	Liver cirrhosis	55.1	23.8
LAK cells IL-2+IL-12	39.2	23.7	Lupus kidney	27.0	0.0
LAK cells IL-2+IFN gamma	50.3	23.8	NCI-H292 none	48.6	**100.0**
LAK cells IL-2+IL-18	26.6	56.3	NCI-H292 IL-4	60.3	59.9
LAK cells PMA/ionomycin	25.2	12.2	NCI-H292 IL-9	65.1	76.3
NK Cells IL-2 rest	28.3	26.2	NCI-H292 IL-13	96.6	54.7
Two Way MLR 3 day	33.0	36.3	NCI-H292 IFN gamma	27.4	26.6
Two Way MLR 5 day	48.6	13.4	HPAEC none	7.0	6.3
Two Way MLR 7 day	0.0	0.0	HPAEC TNF alpha + IL-1 beta	7.5	7.9
PBMC rest	8.0	11.5	Lung fibroblast none	15.5	13.6
PBMC PWM	**100.0**	84.1	Lung fibroblast TNF alpha + IL-1 beta	0.0	6.4
PBMC PHA-L	26.2	11.3	Lung fibroblast IL-4	59.9	18.2
Ramos (B cell) none	6.0	13.1	Lung fibroblast IL-9	25.2	5.8
Ramos (B cell) ionomycin	56.6	20.7	Lung fibroblast IL-13	32.3	28.7
B lymphocytes PWM	23.5	31.9	Lung fibroblast IFN gamma	32.8	14.2
B lymphocytes CD40L and IL-4	0.0	14.6	Dermal fibroblast CCD1070 rest	48.3	16.4
EOL-1 dbcAMP	18.8	18.7	Dermal fibroblast CCD1070 TNF alpha	52.1	40.6
EOL-1 dbcAMP	17.1	29.7	Dermal fibroblast	32.1	7.3

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PMA/ionomycin			CCD1070 IL-1 beta		
Dendritic cells none	13.3	4.8	Dermal fibroblast IFN gamma	9.2	7.9
Dendritic cells LPS	43.2	9.5	Dermal fibroblast IL-4	24.0	27.4
Dendritic cells anti-CD40	13.3	13.0	IBD Colitis 2	0.0	0.0
Monocytes rest	0.0	36.1	IBD Crohn's	7.6	0.0
Monocytes LPS	70.2	28.1	Colon	28.5	81.8
Macrophages rest	29.9	12.9	Lung	0.0	11.6
Macrophages LPS	55.1	8.4	Thymus	59.5	13.3
HUVEC none	0.0	6.0	Kidney	11.3	0.0
HUVEC starved	19.9	5.1			

CNS_neurodegeneration_v1.0 Summary: Ag2606 The GMAC036216_B gene represents a novel G-protein coupled receptor (GPCR) with expression in the brain. This experiment does not show any association of this gene with Alzheimer's disease. However, the GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and α2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the α-adrenergic receptors have been implicated in memory. Therefore this gene may be of use as a small molecule target for the treatment of any of the described diseases.

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment

desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response.

5   The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at

10   alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

15   3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic

20   receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to

25   increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure:

30   indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

340

4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global

5   ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, $p < 0.05$). Similar

10   effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, $p < 0.05$). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 1.2 Summary: Ag1153 Expression of this gene is low/undetectable (CTs > 35) in all

15   of the samples in this panel (data not shown).

Panel 1.3D Summary: Ag2606 Expression of this gene is low/undetectable (CTs > 35) in all of the samples in this panel (data not shown).

Panel 2.2 Summary: Ag2606 Expression of this gene is low/undetectable (CTs > 35) in all of the samples in this panel (data not shown).

20   **Panel 4D Summary:** Ag1153/Ag2606 Results from two experiments using different probe/primer sets show moderate agreement. Expression of the GMAC036216_B gene is highest in NCI-H292 cells and peripheral blood mononuclear cells. Low level expression of this gene was detected in a wide range of cell types of significance in the immune response in health and disease. Therefore, modulation of the activity of this gene or its protein product

25   with a small molecule drug or antibody may alter the functions of these cells and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, or arthritis.

R. GMAC036216_A: GPCR

Expression of gene GMAC036216_A was assessed using the primer-probe sets Ag1646, Ag2373, Ag2498, Ag2605, Ag1120 and Ag1154, described in Tables RA, RB, RC, RD, RE and RF. Results of the RTQ-PCR runs are shown in Tables RG and RH.

5   Table RA. Probe Name Ag1646

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cccagtcatattcttgctgaag-3'	22	483	294
Probe	TET-5'-ctgcccttctgcctaaccaacattgt-3'-TAMRA	26	508	295
Reverse	5'-ctaaacgagccactccaatatg-3'	22	553	296

Table RB. Probe Name Ag2373

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ccacctctgtgtcatccttatg-3'	22	741	297
Probe	TET-5'-tccatccttctttaccttattgaccca-3'-TAMRA	27	771	298
Reverse	5'-aggaatattacgcccaaaatga-3'	22	798	299

Table RC. Probe Name Ag2498

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ccacctctgtgtcatccttatg-3'	22	741	300
Probe	TET-5'-tccatccttctttaccttattgaccca-3'-TAMRA	27	771	301
Reverse	5'-aggaatattacgcccaaaatga-3'	22	798	302

Table RD. Probe Name Ag2605

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cccagtcatattcttgctgaag-3'	22	483	303
Probe	TET-5'-ctgcccttctgcctaaccaacattgt-3'-TAMRA	26	508	304
Reverse	5'-gctaaacgagccactccaatat-3'	22	554	305

Table RE. Probe Name Ag1120

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cccagtcatattcttgctgaag-3'	22	483	306
Probe	TET-5'-ctgcccttctgcctaaccaacattgt-3'-TAMRA	26	508	307
Reverse	5'-ctaaacgagccactccaatatg-3'	22	553	308

Table RF. Probe Name Ag1154

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cccagtcatattcttgctgaag-3'	22	483	309
Probe	TET-5'-ctgcccttctgcctaaccaacattgt-3'-TAMRA	26	508	310
Reverse	5'-ctaaacgagccactccaatatg-3'	22	553	311

Table RG. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1646, Run 167614617	Tissue Name	Rel. Exp.(%) Ag1646, Run 167614617
Liver adenocarcinoma	0.2	Kidney (fetal)	0.2
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.3
Brain (fetal)	**100.0**	Liver	0.6
Brain (whole)	0.0	Liver (fetal)	0.2
Brain (amygdala)	0.1	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.5	Lung	0.0
Brain (hippocampus)	0.1	Lung (fetal)	0.0
Brain (substantia nigra)	0.5	Lung ca. (small cell) LX-1	0.2
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.3
Spinal cord	0.2	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.2	Lung ca. (non-s.cell)	0.0

		NCI-H23	
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.2
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.3	Mammary gland	0.0
Glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.2	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.2	Ovary	0.0
Bone marrow	0.1	Ovarian ca. OVCAR-3	0.1
Thymus	0.0	Ovarian ca. OVCAR-4	0.1
Spleen	0.0	Ovarian ca. OVCAR-5	0.3
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	1.1	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	0.3
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.0
Colon ca.* SW620 (SW480 met)	0.5	Prostate	0.0
Colon ca. HT29	0.4	Prostate ca.* (bone met) PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.2
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.1	Melanoma UACC-62	0.0

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Gastric ca. (liver met) NCI-N87		0.0	Melanoma M14		0.0
Bladder		0.2	Melanoma LOX IMVI		0.0
Trachea		0.0	Melanoma* (met) SK-MEL-5		0.0
Kidney		0.0	Adipose		0.0

Table RH. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2498, Run 158564692	Rel. Exp.(%) Ag2605, Run 164160377	Tissue Name	Rel. Exp.(%) Ag2498, Run 158564692	Rel. Exp.(%) Ag2605, Run 164160377
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	13.5	8.3
Secondary Tr1 act	16.2	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	9.2	0.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	13.0
Primary Th1 act	8.0	7.3	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	1.8	0.0	Microvascular Dermal EC none	17.2	0.0
Primary Tr1 act	10.7	10.1	Microsvasular Dermal EC TNFalpha + IL-1beta	23.3	0.0
Primary Th1 rest	30.6	17.2	Bronchial epithelium TNFalpha + IL1beta	10.6	8.2
Primary Th2 rest	18.6	8.2	Small airway epithelium none	0.0	8.4
Primary Tr1 rest	**100.0**	10.8	Small airway epithelium	6.2	31.0

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			TNFalpha + IL-1beta		
CD45RA CD4 lymphocyte act	6.1	7.2	Coronery artery SMC rest	7.6	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	9.7
Secondary CD8 lymphocyte rest	6.2	0.0	Astrocytes TNFalpha + IL-1beta	3.1	11.8
Secondary CD8 lymphocyte act	5.2	0.0	KU-812 (Basophil) rest	6.7	0.0
CD4 lymphocyte none	0.0	13.5	KU-812 (Basophil) PMA/ionomycin	6.0	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	14.9	6.9
LAK cells rest	4.0	95.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	11.7	0.0
LAK cells IL-2	0.0	17.1	Liver cirrhosis	71.7	62.0
LAK cells IL-2+IL-12	5.7	7.5	Lupus kidney	7.0	6.2
LAK cells IL-2+IFN gamma	7.4	97.3	NCI-H292 none	27.2	7.5
LAK cells IL-2+IL-18	37.1	13.5	NCI-H292 IL-4	24.7	29.3
LAK cells PMA/ionomycin	5.8	0.0	NCI-H292 IL-9	54.0	22.8
NK Cells IL-2 rest	21.3	17.7	NCI-H292 IL-13	0.0	6.3
Two Way MLR 3 day	17.6	19.9	NCI-H292 IFN gamma	0.0	20.7
Two Way MLR 5 day	11.6	7.8	HPAEC none	0.0	0.0
Two Way MLR 7 day	4.5	0.0	HPAEC TNF alpha + IL-1 beta	0.0	25.7
PBMC rest	4.1	10.9	Lung fibroblast none	5.3	12.5
PBMC PWM	20.7	**100.0**	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0

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PBMC PHA-L	6.0	6.0	Lung fibroblast IL-4	7.1	14.5
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	7.9	7.1
Ramos (B cell) ionomycin	21.8	35.8	Lung fibroblast IL-13	0.0	17.0
B lymphocytes PWM	0.0	28.7	Lung fibroblast IFN gamma	0.0	15.7
B lymphocytes CD40L and IL-4	5.3	9.8	Dermal fibroblast CCD1070 rest	5.4	14.1
EOL-1 dbcAMP	10.7	9.0	Dermal fibroblast CCD1070 TNF alpha	57.4	35.8
EOL-1 dbcAMP PMA/ionomycin	6.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	8.4
Dendritic cells none	29.9	7.2	Dermal fibroblast IFN gamma	0.0	23.0
Dendritic cells LPS	10.3	15.2	Dermal fibroblast IL-4	9.6	13.0
Dendritic cells anti-CD40	0.0	31.0	IBD Colitis 2	11.3	0.0
Monocytes rest	29.1	74.7	IBD Crohn's	0.0	0.0
Monocytes LPS	11.1	85.3	Colon	4.4	7.6
Macrophages rest	5.0	40.9	Lung	6.9	6.3
Macrophages LPS	0.0	0.0	Thymus	70.2	25.5
HUVEC none	7.6	9.3	Kidney	0.0	18.2
HUVEC starved	0.0	0.0			

CNS_neurodegeneration_v1.0 Summary: Ag1646 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel due to a probable probe or chemistry failure (data not shown). Ag2373/Ag2498/Ag2605 Expression of this gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

Panel 1.2 Summary: Ag1120/Ag1154 Results from three experiments using the same probe/primer set show many discrepancies and no conclusions can be drawn from this data (data not shown).

Panel 1.3D Summary: Ag1646 Expression of the GMAC036216_A gene is highest in fetal brain (CT = 29). Interestingly, this gene does not appear to be as highly expressed in adult brain. This result suggests that expression of this gene may be used to distinguish fetal from

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adult brain. In addition, this gene product may be useful in regeneration of brain tissue. Ag2373/Ag2498/Ag2605 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag1646/Ag2373 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag2498/Ag2605 Results from experiments using two different probe/primer sets do not correlate well with one another. In the experiment using Ag2498, the GMAC036216_A gene is most highly expressed in the thymus and in primary regulatory T cells (Tr1). This transcript may encode a receptor involved in differentiation, activation or the regulatory activity of T cells. Therefore, antagonistic or agonistic antibodies, small molecule or protein therapeutics may be able to regulate immune responses and be important for organ transplant (antagonistic) and cancer therapeutics (agonistic). In the experiment using Ag2605, xpression of this gene is seen at low levels across a number of tissues on this panel. Highest expression of the GMAC036216_A gene is seen in peripheral blood mononuclear cells (PBMC) treated with poke weed mitogen and in lymphokine-activated killer cells (LAKs) (CTs = 32.5). Interestingly, expression of this gene is upregulated in Ramos B cells treated with ionomycin (CT = 34) when compared to expression in resting Ramos B cells (CT = 40); therefore, expression of this gene could be used to distinguish between these two samples. Additional low but significant expression of this gene is also seen in monocytes, macrophages, and liver cirrhosis. Thus, therapeutic modulation of this gene or its protein product, using small molecule drugs, antibodies, or protein therapeutics, could be of use in the treatment of a variety of autoimmune and inflammatory diseases such as asthma, allergies, liver cirrhosis, inflammatory bowel disease, lupus erythematosus, or arthritis. Ag1120/Ag2373/Ag1646 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel CNS_1 Summary: Ag1646 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

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S. GMAC026090_C: GPCR

Expression of gene GMAC026090_C was assessed using the primer-probe set Ag2603, described in Table SA. Results of the RTQ-PCR runs are shown in Tables SB, SC, SD and SE.

Table SA. Probe Name Ag2603

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tgtactacttcttggccatgct-3'	22	189	312
Probe	TET-5'-tagtacaatccctaaagccctctgca-3'-TAMRA	26	238	313
Reverse	5'-tccttgagatgaaaccagaaga-3'	22	264	314

Table SB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2603, Run 208779994	Tissue Name	Rel. Exp.(%) Ag2603, Run 208779994
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	3.6
AD 2 Hippo	7.9	Control (Path) 4 Temporal Ctx	26.8
AD 3 Hippo	0.0	AD 1 Occipital Ctx	3.1
AD 4 Hippo	3.4	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	0.0	AD 3 Occipital Ctx	0.0
AD 6 Hippo	57.4	AD 4 Occipital Ctx	11.5
Control 2 Hippo	13.5	AD 5 Occipital Ctx	16.8
Control 4 Hippo	1.9	AD 5 Occipital Ctx	0.0
Control (Path) 3 Hippo	3.6	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	7.5	Control 2 Occipital Ctx	7.1
AD 2 Temporal Ctx	2.1	Control 3 Occipital Ctx	7.1
AD 3 Temporal Ctx	3.2	Control 4 Occipital Ctx	2.8
AD 4 Temporal Ctx	5.5	Control (Path) 1 Occipital Ctx	30.4
AD 5 Inf Temporal Ctx	33.0	Control (Path) 2 Occipital Ctx	3.1
AD 5 Sup	26.8	Control (Path) 3	8.7

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Temporal Ctx		Occipital Ctx	
AD 6 Inf Temporal Ctx	**100.0**	Control (Path) 4 Occipital Ctx	3.7
AD 6 Sup Temporal Ctx	54.0	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	3.8
Control 2 Temporal Ctx	17.0	Control 3 Parietal Ctx	16.3
Control 3 Temporal Ctx	9.6	Control (Path) 1 Parietal Ctx	17.4
Control 3 Temporal Ctx	0.0	Control (Path) 2 Parietal Ctx	3.8
Control (Path) 1 Temporal Ctx	32.1	Control (Path) 3 Parietal Ctx	6.5
Control (Path) 2 Temporal Ctx	11.0	Control (Path) 4 Parietal Ctx	13.3

Table SC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2603, Run 166219800	Tissue Name	Rel. Exp.(%) Ag2603, Run 166219800
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	6.8	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	6.7	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	11.0	Renal ca. UO-31	8.0
Pituitary gland	6.5	Renal ca. TK-10	0.0
Brain (fetal)	12.9	Liver	0.0
Brain (whole)	7.3	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	6.9	Lung	62.9
Brain (hippocampus)	7.4	Lung (fetal)	13.5
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	32.1	Lung ca. (large	0.0

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		cell)NCI-H460	
Glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	8.5
Glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	5.9
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	8.8	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	30.8
glioma U251	8.8	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	15.0
Heart	17.6	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	23.0	Ovarian ca. OVCAR-3	0.0
Thymus	44.1	Ovarian ca. OVCAR-4	0.0
Spleen	8.5	Ovarian ca. OVCAR-5	0.0
Lymph node	74.2	Ovarian ca. OVCAR-8	0.0
Colorectal	50.3	Ovarian ca. IGROV-1	4.7
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	**100.0**
Small intestine	29.9	Uterus	2.2
Colon ca. SW480	0.0	Placenta	34.9
Colon ca.* SW620 (SW480 met)	0.0	Prostate	18.8
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	0.0
Colon ca. HCT-116	0.0	Testis	20.2
Colon ca. CaCo-2	0.0	Melanoma	0.0

		Hs688(A).T	
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	8.9
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	47.0	Melanoma LOX IMVI	0.0
Trachea	15.4	Melanoma* (met) SK-MEL-5	0.0
Kidney	8.5	Adipose	31.9

Table SD. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag2603, Run 175127862	Tissue Name	Rel. Exp.(%) Ag2603, Run 175127862
Normal Colon	3.5	Kidney Margin (OD04348)	**100.0**
Colon cancer (OD06064)	4.9	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	2.9	Kidney normal adjacent tissue (OD06204E)	7.7
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	11.9	Kidney Margin (OD04450-03)	10.9
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	4.2	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	2.9
CC Margin (ODO3921)	5.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	9.8	Kidney Margin 8120608	2.7
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	4.7
Lung Margin (OD04451-02)	24.8	Uterine Cancer 064011	5.4
Normal Prostate	5.5	Normal Thyroid	4.1

Prostate Cancer (OD04410)	3.2	Thyroid Cancer	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	2.2	Normal Breast	26.8
Ovarian Margin (OD06283-07)	27.9	Breast Cancer	7.5
Ovarian Cancer	10.1	Breast Cancer	3.4
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	13.9	Breast Cancer Mets (OD04590-03)	4.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis	0.0
Ovarian Margin (OD06455-07)	22.2	Breast Cancer	0.0
Normal Lung	9.0	Breast Cancer 9100266	3.1
Invasive poor diff. lung adeno (ODO4945-01	19.9	Breast Margin 9100265	3.2
Lung Margin (ODO4945-03)	65.5	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	4.0
Lung Margin (OD03126)	1.4	Breast cancer (OD06083)	8.0
Lung Cancer (OD05014A)	4.8	Breast cancer node metastasis (OD06083)	11.6
Lung Margin (OD05014B)	7.9	Normal Liver	0.0
Lung cancer (OD06081)	3.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	3.1	Liver Cancer 1025	11.4
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	11.0
Lung Margin (OD04237-02)	20.2	Liver Tissue 6004-N	5.8
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0
Liver Margin (ODO4310)	0.0	Liver Tissue 6005-N	7.5
Melanoma Metastasis	0.0	Liver Cancer	18.0

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Lung Margin (OD04321)	4.5	Normal Bladder	8.5
Normal Kidney	0.0	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	4.4	Bladder Cancer	22.5
Kidney Margin (OD04338)	5.0	Normal Stomach	21.3
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	5.4
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	5.7
Kidney Ca, Clear cell type (OD04340)	8.4	Gastric Cancer 9060395	7.9
Kidney Margin (OD04340)	8.7	Stomach Margin 9060394	4.5
Kidney Ca, Nuclear grade 3 (OD04348)	15.1	Gastric Cancer 064005	13.7

Table SE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2603, Run 164160188	Tissue Name	Rel. Exp.(%) Ag2603, Run 164160188
Secondary Th1 act	0.0	HUVEC IL-1beta	1.5
Secondary Th2 act	5.7	HUVEC IFN gamma	2.8
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	10.4	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	3.1	HUVEC IL-11	0.0
Secondary Tr1 rest	9.6	Lung Microvascular EC none	1.5
Primary Th1 act	1.9	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	5.3	Microvascular Dermal EC none	0.0
Primary Tr1 act	10.2	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	65.1	Bronchial epithelium TNFalpha + IL1beta	6.5
Primary Th2 rest	13.7	Small airway epithelium none	0.0
Primary Tr1 rest	12.3	Small airway epithelium TNFalpha + IL-1beta	7.4
CD45RA CD4	15.8	Coronery artery SMC rest	0.0

lymphocyte act			
CD45RO CD4 lymphocyte act	29.9	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	6.3	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	42.9	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	2.4	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	35.1	KU-812 (Basophil) PMA/ionomycin	1.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	14.2	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	32.1	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	1.3
LAK cells IL-2	80.7	Liver cirrhosis	17.4
LAK cells IL-2+IL-12	81.2	Lupus kidney	3.1
LAK cells IL-2+IFN gamma	100.0	NCI-H292 none	1.4
LAK cells IL-2+ IL-18	95.9	NCI-H292 IL-4	0.7
LAK cells PMA/ionomycin	6.7	NCI-H292 IL-9	2.1
NK Cells IL-2 rest	32.8	NCI-H292 IL-13	0.0
Two Way MLR 3 day	66.0	NCI-H292 IFN gamma	1.1
Two Way MLR 5 day	19.9	HPAEC none	0.0
Two Way MLR 7 day	10.1	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	5.9	Lung fibroblast none	0.0
PBMC PWM	66.4	Lung fibroblast TNF alpha + IL-1 beta	0.9
PBMC PHA-L	9.9	Lung fibroblast IL-4	0.3
Ramos (B cell) none	0.0	Lung fibroblast IL-9	2.8
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	1.0
B lymphocytes PWM	9.2	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	9.7	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	3.1	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	16.5	Dermal fibroblast IFN gamma	0.0

Dendritic cells LPS	6.5	Dermal fibroblast IL-4	6.1
Dendritic cells anti-CD40	3.0	IBD Colitis 2	6.0
Monocytes rest	5.4	IBD Crohn's	1.0
Monocytes LPS	3.2	Colon	15.2
Macrophages rest	18.2	Lung	5.3
Macrophages LPS	10.4	Thymus	8.4
HUVEC none	0.0	Kidney	52.5
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: <u>Ag2603</u> The GMAC026090_C gene encodes a novel G-protein coupled receptor (GPCR) with expression in the brain. The GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and α2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the α-adrenergic receptors have been implicated in memory. Therefore this gene may be of use as a small molecule target for the treatment of any of the described diseases.

Furthermore, the expression of this GPCR is found to be upregulated in the temporal cortex of Alzheimer's disease patients. Thus, blockade of this receptor may be of use in the treatment of this disease and decrease neuronal death.

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment

desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response.

5   The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at

10   alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

15   3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic

20   receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to

25   increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure:

30   indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

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4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, $p < 0.05$). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, $p < 0.05$). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 1.3D Summary: <u>Ag2603</u> Expression of the GMAC026090_C gene is highest in an ovarian cancer cell line (CT = 33.6). Low but significant expression is also detected in lymph node, lung, colon and bladder. Therefore, expression of this gene may be used to distinguish these tissues from the other samples on this panel.

Panel 2.2 Summary: <u>Ag2603</u> Highest expression of the GMAC026090_C gene is seen in a sample derived from normal kidney adjacent to a tumor (CT=32.9). Significant expression is also seen in normal lung tissue adjacent to a tissue. Thus, expression of this gene could be used to differentiate these tissues from other samples on this panel.

Panel 4D Summary: <u>Ag2603</u> The GMAC026090_C gene is expressed at moderate to low levels in a wide range of cell types and normal tissues involved in immune response. Highest expression of this gene is seen in stimulated lymphokine-activated killer cells (LAK)(CT=30.1). These cells are involved in tumor immunology and cell clearance of tumors and virally and bacterial infected cells. Therefore, modulation of the function of this gene product with a small molecule drug or antibody may alter the functions of these cells and lead to improvement of symptoms associated with these conditions.

Low level expression of this gene is also detected in dendritic cells, monocytes, macrophages, stimulated PBMCs, and primary T cells. Therefore, modulation of the function

of this gene product with a small molecule drug or antibody may alter the functions of B cells, cells of the T-cell lineage, macrophages and monocytes and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, arthritis, and cancer-related conditions.

T. GMAC026090_B: GPCR

Expression of gene GMAC026090_B was assessed using the primer-probe set Ag2602, described in Table TA. Results of the RTQ-PCR runs are shown in Table TB.

Table TA. Probe Name Ag2602

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gtgctgagaaatggcttatttg-3'	22	487	315
Probe	TET-5'-cactccagtgcctgtgcttgcag-3'-TAMRA	23	510	316
Reverse	5'-tcaatttcattcttggagcaat-3'	22	545	317

Table TB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2602, Run 164216249	Tissue Name	Rel. Exp.(%) Ag2602, Run 164216249
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	5.1	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	6.8	HUVEC TNF alpha + IL4	1.8
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	1.8	Lung Microvascular EC none	2.4
Primary Th1 act	2.6	Lung Microvascular EC TNFalpha + IL-1beta	1.4
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	49.7	Bronchial epithelium	0.0

		TNFalpha + IL1beta	
Primary Th2 rest	23.2	Small airway epithelium none	0.0
Primary Tr1 rest	3.8	Small airway epithelium TNFalpha + IL-1beta	1.2
CD45RA CD4 lymphocyte act	2.5	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	14.9	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	3.2	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	18.8	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	1.6
CD4 lymphocyte none	13.9	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	1.9	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	11.5	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	33.9	Liver cirrhosis	7.1
LAK cells IL-2+IL-12	24.1	Lupus kidney	3.6
LAK cells IL-2+IFN gamma	**100.0**	NCI-H292 none	1.4
LAK cells IL-2+ IL-18	34.2	NCI-H292 IL-4	1.3
LAK cells PMA/ionomycin	4.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	11.2	NCI-H292 IL-13	0.0
Two Way MLR 3 day	32.1	NCI-H292 IFN gamma	2.4
Two Way MLR 5 day	2.1	HPAEC none	0.0
Two Way MLR 7 day	3.3	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	1.3	Lung fibroblast none	2.1
PBMC PWM	25.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	14.6	Lung fibroblast IL-4	1.2
Ramos (B cell) none	0.0	Lung fibroblast IL-9	3.5
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	27.9	Lung fibroblast IFN gamma	4.0
B lymphocytes CD40L and IL-4	7.3	Dermal fibroblast CCD1070 rest	0.0

EOL-1 dbcAMP	1.4	Dermal fibroblast CCD1070 TNF alpha	12.2
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	3.1	Dermal fibroblast IFN gamma	2.7
Dendritic cells LPS	3.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	1.5	IBD Colitis 2	1.5
Monocytes rest	1.7	IBD Crohn's	0.0
Monocytes LPS	1.8	Colon	11.7
Macrophages rest	6.0	Lung	4.8
Macrophages LPS	0.0	Thymus	3.6
HUVEC none	1.3	Kidney	16.7
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag2602 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag2602 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag2602 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag2602 Expression of the GMAC026090_B gene is seen in stimulated lymphokine-activated killer cells (LAKs) (CT = 33.5). These cells are involved in tumor immunology and cell clearance of tumors and virally and bacterial infected cells. Therefore, modulation of the function of this gene product with a small molecule drug or antibody may alter the functions of these cells and lead to improvement of symptoms associated with these conditions. Low but significant expression is also detected in resting primary T cells (CT = 34.5). Expression of this gene could also be used to distinguish these two samples from the other samples on this panel.

U. GMAC026090_A: GPCR

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Expression of gene GMAC026090_A was assessed using the primer-probe set Ag2601, described in Table UA. Results of the RTQ-PCR runs are shown in Table UB.

Table UA. Probe Name Ag2601

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tcccacctcatcttaatcctttt-3'	22	694	318
Probe	TET-5'-cacagtcatcattgtgatttccattactcg-3'-TAMRA	30	723	319
Reverse	5'-tggaataaggggaactctcatt-3'	22	762	320

Table UB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2601, Run 164160032	Tissue Name	Rel. Exp.(%) Ag2601, Run 164160032
Secondary Th1 act	3.2	HUVEC IL-1beta	7.6
Secondary Th2 act	10.7	HUVEC IFN gamma	0.0
Secondary Tr1 act	2.9	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	5.0	HUVEC IL-11	0.0
Secondary Tr1 rest	18.6	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	6.2
Primary Th2 act	2.8	Microvascular Dermal EC none	0.0
Primary Tr1 act	3.3	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	46.7	Bronchial epithelium TNFalpha + IL1beta	1.2
Primary Th2 rest	3.7	Small airway epithelium none	4.9
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	15.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	11.7	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	8.2	Astrocytes rest	2.4
Secondary CD8	21.6	Astrocytes TNFalpha +	0.0

lymphocyte rest		IL-1beta	
Secondary CD8 lymphocyte act	4.4	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	8.5	KU-812 (Basophil) PMA/ionomycin	16.2
2ry Th1/Th2/Tr1_anti-CD95 CH11	2.1	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	30.8	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	30.4	Liver cirrhosis	52.5
LAK cells IL-2+IL-12	41.2	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	**100.0**	NCI-H292 none	0.9
LAK cells IL-2+ IL-18	40.1	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	7.3	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	8.7	NCI-H292 IL-13	0.0
Two Way MLR 3 day	7.6	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	5.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	9.9	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	8.2	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	13.3	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	2.8	Dermal fibroblast CCD1070 TNF alpha	4.7
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	12.4	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	5.8	Dermal fibroblast IL-4	4.5
Dendritic cells anti-CD40	0.0	IBD Colitis 2	1.2
Monocytes rest	2.5	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	4.0

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Macrophages rest	11.8	Lung	0.0
Macrophages LPS	1.7	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag2601 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag2601 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag2601 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag2601 Expression of the GMAC026090_A gene is highest in stimulated lymphokine-activated killer cells (LAKs) (CT = 32.1). These cells are involved in tumor immunology and cell clearance of tumors and virally and bacterial infected cells. Therefore, modulation of the function of this gene product with a small molecule drug or antibody may alter the functions of these cells and lead to improvement of symptoms associated with these conditions. Low but significant expression is also detected in resting primary T cells (CT = 33.2) and liver cirrhosis (CT = 33), suggesting a potential role for this gene in T cell-mediated diseases and liver cirrhosis. Expression of this gene could also be used to distinguish these samples from the other samples on this panel.

V. GMAP002358_A: GPCR

Expression of gene GMAP002358_A was assessed using the primer-probe set Ag2200, described in Table VA. Results of the RTQ-PCR runs are shown in Tables VB.

Table VA. Probe Name Ag2200

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tatttcatcctgctgggattct-3'	22	37	321
Probe	TET-5'-tcccaggatcataaaagtgctcttca-3'-TAMRA	26	66	322
Reverse	5'-tccaggccagagatgtaatgta-3'	22	109	323

Table VB. Panel 2D

Tissue Name	Rel. Exp.(%) Ag2200, Run 164025299	Tissue Name	Rel. Exp.(%) Ag2200, Run 164025299
Normal Colon	0.1	Kidney Margin 8120608	0.0
CC Well to Mod Diff (ODO3866)	1.3	Kidney Cancer 8120613	0.0
CC Margin (ODO3866)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 rectosigmoid (ODO3868)	0.0	Kidney Cancer 9010320	0.2
CC Margin (ODO3868)	0.0	Kidney Margin 9010321	0.0
CC Mod Diff (ODO3920)	0.0	Normal Uterus	0.0
CC Margin (ODO3920)	0.0	Uterine Cancer 064011	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Normal Thyroid	0.0
CC Margin (ODO3921)	0.2	Thyroid Cancer	2.8
CC from Partial Hepatectomy (ODO4309) Mets	0.2	Thyroid Cancer A302152	100.0
Liver Margin (ODO4309)	0.8	Thyroid Margin A302153	0.0
Colon mets to lung (OD04451-01)	0.4	Normal Breast	0.0
Lung Margin (OD04451-02)	0.0	Breast Cancer	0.4
Normal Prostate 6546-1	0.0	Breast Cancer (OD04590-01)	0.4
Prostate Cancer (OD04410)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Prostate Margin (OD04410)	0.0	Breast Cancer Metastasis	0.0
Prostate Cancer (OD04720-01)	0.0	Breast Cancer	0.0
Prostate Margin (OD04720-02)	0.0	Breast Cancer	0.0
Normal Lung	0.6	Breast Cancer 9100266	0.0
Lung Met to Muscle	0.3	Breast Margin	0.0

(ODO4286)		9100265	
Muscle Margin (ODO4286)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.2
Lung Margin (OD03126)	0.0	Normal Liver	0.8
Lung Cancer (OD04404)	0.3	Liver Cancer	0.4
Lung Margin (OD04404)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04565)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD04565)	0.1	Liver Cancer 6004-T	0.6
Lung Cancer (OD04237-01)	0.0	Liver Tissue 6004-N	0.2
Lung Margin (OD04237-02)	0.0	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	0.0	Normal Bladder	0.0
Melanoma Metastasis	0.2	Bladder Cancer	0.2
Lung Margin (OD04321)	0.0	Bladder Cancer	1.6
Normal Kidney	0.0	Bladder Cancer (OD04718-01)	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	10.5	Bladder Normal Adjacent (OD04718-03)	0.0
Kidney Margin (OD04338)	0.0	Normal Ovary	0.0
Kidney Ca Nuclear grade ½ (OD04339)	0.4	Ovarian Cancer	0.0
Kidney Margin (OD04339)	0.0	Ovarian Cancer (OD04768-07)	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Ovary Margin (OD04768-08)	0.0
Kidney Margin (OD04340)	0.2	Normal Stomach	0.3
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 9060358	0.0
Kidney Margin (OD04348)	0.3	Stomach Margin 9060359	0.3
Kidney Cancer (OD04622-01)	0.8	Gastric Cancer 9060395	0.0
Kidney Margin (OD04622-03)	0.0	Stomach Margin 9060394	0.0

Kidney Cancer (OD04450-01)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04450-03)	0.0	Stomach Margin 9060396	0.0
Kidney Cancer 8120607	0.0	Gastric Cancer 064005	0.5

CNS_neurodegeneration_v1.0   Summary: <u>Ag2200</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: <u>Ag2200</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2D Summary: <u>Ag2200</u> The GMAP002358_A gene is most highly expressed in a thyroid cancer sample (CT = 29). Interestingly, expression of this gene is not detectable in the matched adjacent normal thyroid tissue. This gene is also expressed at low but significant levels in an additional thyroid tumor. Therefore, expression of this gene may be used to distinguish thyroid cancer from normal thyroid tissue. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene, using small molecule drugs or antibodies, may be beneficial in the treatment of thyroid cancer.

Panel 3D Summary: <u>Ag2200</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag2200</u> Results cannot be evaluated due to potential problems with some of the samples in this particular experiment; suspicious amp plot (data not shown).

W. GMAP002517_C: GPCR

Expression of gene GMAP002517_C was assessed using the primer-probe set Ag1839, described in Table WA. Results of the RTQ-PCR runs are shown in Table WB.

<u>Table WA</u>. Probe Name Ag1839

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tgaacctcatggctgagaataa-3'	22	261	324

| Probe | TET-5'-atttcttttcatggatgtgctgccca-3'-TAMRA | 26 | 287 | 325 |
| Reverse | 5'-ggaaggagccaaagaagtagaa-3' | 22 | 314 | 326 |

Table WB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1839, Run 165831028	Tissue Name	Rel. Exp.(%) Ag1839, Run 165831028
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	1.2	HUVEC IFN gamma	0.0
Secondary Tr1 act	2.7	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**

LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	2.2
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	3.8	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	19.6
Monocytes rest	0.0	IBD Crohn's	3.5
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.8	Thymus	2.5
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1839 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: <u>Ag1839</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag1839</u> Significant expression of the GMAP002517_C gene is detected in a liver cirrhosis sample (CT = 32). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

X. GMAP002517_B: GPCR

Expression of gene GMAP002517_B was assessed using the primer-probe set Ag1838, described in Table XA. Results of the RTQ-PCR runs are shown in Table XB.

<u>Table XA</u>. Probe Name Ag1838

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atccagtgtcatcaaccacttc-3'	22	510	327
Probe	TET-5'-cgccgctcattaagctttcttgttct-3'-TAMRA	26	545	328
Reverse	5'-gatatgaacatggcatgctctt-3'	22	584	329

<u>Table XB</u>. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1838, Run 165828676	Tissue Name	Rel. Exp.(%) Ag1838, Run 165828676
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0

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Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	2.7	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	1.2
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	1.3
Ramos (B cell)	0.0	Lung fibroblast IL-13	0.0

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ionomycin			
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	5.1
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	9.5
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	13.8
Monocytes rest	0.0	IBD Crohn's	7.3
Monocytes LPS	0.0	Colon	4.5
Macrophages rest	0.0	Lung	3.2
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1838 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag1838 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1838 Significant expression of the GMAP002517_B gene is detected in a liver cirrhosis sample (CT = 32.7). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

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Y. GMAP002418_E: GPCR

Expression of gene GMAP002418_E was assessed using the primer-probe set
Ag1837, described in Table YA. Results of the RTQ-PCR runs are shown in Tables YB and
YC.

5   Table YA. Probe Name Ag1837

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ctgcatctctgaagacaaaagc-3'	22	251	330
Probe	TET-5'-tggctgcctgtgtcagttcttcttct-3'-TAMRA	26	284	331
Reverse	5'-gccagtaagcagcactcactat-3'	22	325	332

Table YB. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag1837, Run 174148648	Tissue Name	Rel. Exp.(%) Ag1837, Run 174148648
Normal Colon	0.0	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	7.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	4.0	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	0.0

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Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer	0.0
Ovarian Cancer	5.2	Breast Cancer	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	0.0
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	0.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	5.3
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0

Liver Margin (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	**100.0**	Liver Cancer	7.6
Lung Margin (OD04321)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	1.8
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table YC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1837, Run 165830925	Tissue Name	Rel. Exp.(%) Ag1837, Run 165830925
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	6.7	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0

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Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	7.1
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast	0.0

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PMA/ionomycin		CCD1070 IL-1 beta	
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	21.9
Monocytes rest	0.0	IBD Crohn's	7.1
Monocytes LPS	0.0	Colon	17.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: <u>Ag1837</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: <u>Ag1837</u> Significant expression of the GMAP002418_E gene is seen exclusively in a sample from a melanoma metastasis (CT = 33.2). Therefore, expression of this gene may be used to distinguish metastatic melanomas from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of metastatic melanoma.

Panel 4D Summary: <u>Ag1837</u> Significant expression of the GMAP002418_E gene is detected in a liver cirrhosis sample (CT = 34.5). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

Z. GMAP002418_B/CG149702-01: Olfactory Receptor

Expression of gene GMAP002418_B (also known as CG149702-01) was assessed using the primer-probe set Ag1835, described in Table ZA. Results of the RTQ-PCR runs are shown in Tables ZB, ZC and ZD.

<u>Table ZA.</u> Probe Name Ag1835

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Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ccttctggatctctggtattcc-3'	22	231	333
Probe	TET-5'-atccccgatatcctgctgacttgcat-3'-TAMRA	26	262	334
Reverse	5'-ggagatggttttgtcatcagaa-3'	22	288	335

Table ZB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1835, Run 165981806	Tissue Name	Rel. Exp.(%) Ag1835, Run 165981806
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	14.5	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	**100.0**	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	8.2	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0

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astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	18.7
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.0
Colon ca.* SW620 (SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Tissue Name	Rel. Exp.(%) Ag1835, Run 165828257	Tissue Name	Rel. Exp.(%) Ag1835, Run 165828257
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	4.6	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	2.1
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	7.2	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0

LAK cells IL-2+ IL-18	3.7	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	1.4	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	2.6	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	75.3	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	8.4
Monocytes rest	0.0	IBD Crohn's	7.3
Monocytes LPS	0.0	Colon	12.1
Macrophages rest	0.0	Lung	3.2
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: <u>Ag1835</u> Significant expression of the GMAP002418_B gene is seen exclusively in a sample from an astrocytoma cell line (CT = 34). Therefore, expression of this gene may be used to distinguish astrocytoma cell lines from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may

5   be beneficial in the treatment of astrocytomas.

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Panel 2.2 Summary: <u>Ag1835</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag1835</u> Expression of the GMAP002418_B gene is highest in a liver cirrhosis sample (CT = 32.4). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis. Low but significant expression of this gene is also seen in activated EOL-1 eosinophil cells (CT=32.9). Due to the importance of eosinophils in lung pathology and primary biliary cirrhosis, antibody or small molecule therapies designed with the protein encoded for by this gene could block or inhibit inflammation or tissue damage due to lung conditions including asthma, allergies, hypersensitivity reactions, and viral infections. Expression of this gene could also be used to distinguish liver cirrhosis and activated eosinophils from the other samples on this panel.

AA. GMAP002345_C: GPCR

Expression of gene GMAP002345_C was assessed using the primer-probe sets Ag1732 and Ag1833, described in Tables AAA and AAB. Results of the RTQ-PCR runs are shown in Tables AAC, AAD and AAE.

<u>Table AAA</u>. Probe Name Ag1732

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gacaaaatggcatctgtgttct-3'	22	819	336
Probe	TET-5'-agtcattcccatgttgaatccactgg-3'-TAMRA	26	848	337
Reverse	5'-tctttgttcctcaggctgtaga-3'	22	874	338

<u>Table AAB</u>. Probe Name Ag1833

Primers	Sequences	Length	Start Position	SEQ ID NO:

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Forward	5'-gacaaaatggcatctgtgttct-3'	22	819	339
Probe	TET-5'-agtcattcccatgttgaatccactgg-3'-TAMRA	26	848	340
Reverse	5'-tctttgttcctcaggctgtaga-3'	22	874	341

Table AAC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1833, Run 165975011	Tissue Name	Rel. Exp.(%) Ag1833, Run 165975011
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	25.9	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	19.9
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	6.9
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	25.9	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	28.1
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	18.6	Mammary gland	0.0

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glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (Fetal)	0.0	Breast ca.* (pl. ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (Fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. (ascites) SK-OV-3	66.4
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.0
Colon ca.* SW620 (SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
CC Well to Mod Diff (ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca. (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table AAD. Panel 2.2

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Tissue Name	Rel. Exp.(%) Ag1732, Run 173761943	Rel. Exp.(%) Ag1833, Run 174229569	Tissue Name	Rel. Exp.(%) Ag1732, Run 173761943	Rel. Exp.(%) Ag1833, Run 174229569
Normal Colon	0.0	0.0	Kidney Margin (OD04348)	0.0	0.0
Colon cancer (OD06064)	0.0	0.0	Kidney malignant cancer (OD06204B)	0.0	0.0
Colon Margin (OD06064)	0.0	0.0	Kidney normal adjacent tissue (OD06204E)	0.0	0.0
Colon cancer (OD06159)	0.0	0.0	Kidney Cancer (OD04450-01)	0.0	0.0
Colon Margin (OD06159)	0.0	0.0	Kidney Margin (OD04450-03)	0.0	0.0
Colon cancer (OD06297-04)	0.0	0.0	Kidney Cancer 8120613	0.0	0.0
Colon Margin (OD06297-015)	0.0	0.0	Kidney Margin 8120614	0.0	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	0.0	Kidney Cancer 9010320	0.0	0.0
CC Margin (ODO3921)	0.0	0.0	Kidney Margin 9010321	0.0	0.0
Colon cancer metastasis (OD06104)	0.0	0.0	Kidney Cancer 8120607	0.0	0.0
Lung Margin (OD06104)	0.0	0.0	Kidney Margin 8120608	0.0	0.0
Colon mets to lung (OD04451-01)	0.0	0.0	Normal Uterus	0.0	0.0
Lung Margin (OD04451-02)	0.0	0.0	Uterine Cancer 064011	0.0	0.0
Normal Prostate	0.0	0.0	Normal Thyroid	0.0	0.0
Prostate Cancer (OD04410)	3.2	0.0	Thyroid Cancer	0.0	0.0
Prostate Margin (OD04410)	0.0	0.0	Thyroid Cancer A302152	0.0	0.0
Normal Ovary	0.0	0.0	Thyroid Margin A302153	0.0	0.0
Ovarian cancer (OD06283-03)	0.0	0.0	Normal Breast	0.0	0.0
Ovarian Margin	0.0	38.4	Breast Cancer	16.7	0.0

(OD06283-07)					
Ovarian Cancer	**100.0**	**100.0**	Breast Cancer	12.2	0.0
Ovarian cancer (OD06145)	0.0	0.0	Breast Cancer (OD04590-01)	0.0	0.0
Ovarian Margin (OD06145)	0.0	0.0	Breast Cancer Mets (OD04590-03)	0.0	0.0
Ovarian cancer (OD06455-03)	0.0	0.0	Breast Cancer Metastasis	0.0	0.0
Ovarian Margin (OD06455-07)	0.0	0.0	Breast Cancer	0.0	0.0
Normal Lung	0.0	0.0	Breast Cancer 9100266	0.0	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	0.0	Breast Margin 9100265	0.0	0.0
Lung Margin (ODO4945-03)	0.0	0.0	Breast Cancer A209073	0.0	0.0
Lung Malignant Cancer (OD03126)	12.8	0.0	Breast Margin A2090734	0.0	0.0
Lung Margin (OD03126)	0.0	0.0	Breast cancer (OD06083)	0.0	0.0
Lung Cancer (OD05014A)	0.0	0.0	Breast cancer node metastasis (OD06083)	0.0	0.0
Lung Margin (OD05014B)	0.0	0.0	Normal Liver	0.0	0.0
Lung cancer (OD06081)	0.0	0.0	Liver Cancer 1026	0.0	0.0
Lung Margin (OD06081)	0.0	0.0	Liver Cancer 1025	2.8	0.0
Lung Cancer (OD04237-01)	0.0	0.0	Liver Cancer 6004-T	0.0	0.0
Lung Margin (OD04237-02)	0.0	0.0	Liver Tissue 6004-N	0.0	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	0.0	Liver Cancer 6005-T	0.0	0.0
Liver Margin (ODO4310)	0.0	0.0	Liver Tissue 6005-N	0.0	0.0
Melanoma Metastasis	0.0	0.0	Liver Cancer	0.0	0.0
Lung Margin	0.0	0.0	Normal Bladder	0.0	0.0

(OD04321)					
Normal Kidney	0.0	0.0	Bladder Cancer	0.0	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	2.2	0.0	Bladder Cancer	0.0	0.0
Kidney Margin (OD04338)	0.0	0.0	Normal Stomach	0.0	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	0.0	Gastric Cancer 9060397	0.0	0.0
Kidney Margin (OD04339)	0.0	0.0	Stomach Margin 9060396	0.0	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	0.0	Gastric Cancer 9060395	21.8	0.0
Kidney Margin (OD04340)	0.0	0.0	Stomach Margin 9060394	0.0	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	0.0	Gastric Cancer 064005	0.0	0.0

Table AAE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1833, Run 165824840	Tissue Name	Rel. Exp.(%) Ag1833, Run 165824840
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	2.9

Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	2.6	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	11.7	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	1.9	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	2.7	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	1.4	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	10.3	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast	12.5

		CCD1070 TNF alpha	
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.9
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	1.3	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: <u>Ag1833</u> Expression of the GMAP002345_C gene is highest (CT = 33.9) in the spleen, an important site of secondary immune responses. Therefore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases. In addition, low but significant expression of this gene is also detected in an ovarian cancer cell line (CT = 34.5). <u>Ag1732</u> Data from a second experiment with Ag1732 is not included because the amp plot suggests that there were experimental difficulties with this run.

Panel 2.2 Summary: <u>Ag1732/Ag1833</u> Results from two experiments using an identical probe/primer set are very comparable. Significant expression of the GMAP002345_C gene is limited to a single ovarian cancer sample in this panel. These results are consistent with what was seen in Panel 1.3D. Therefore, expression of this gene may be used to distinguish ovarian cancers from the other samples on this panel. Furthermore, therapeutic modulation of the GPCR encoded by this gene, using small molecule drugs or antibodies, may be beneficial in the treatment of ovarian cancer.

Panel 4D Summary: <u>Ag1833</u> Significant expression of the GMAP002345_C gene is detected in a liver cirrhosis sample (CT = 32.5). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition,

antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis. Ag1732 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5   AB. GMAP002345_A: GPCR

Expression of gene GMAP002345_A was assessed using the primer-probe sets Ag1730 and Ag1830, described in Tables ABA and ABB. Results of the RTQ-PCR runs are shown in Tables ABC and ABD.

Table ABA. Probe Name Ag1730

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tgatcctgatggactcttgtct-3'	22	146	342
Probe	TET-5'-ttcctcagtaacctgtctctggtgga-3'-TAMRA	26	187	343
Reverse	5'-agtgacagctgaggagtatcca-3'	22	216	344

10   Table ABB. Probe Name Ag1830

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gacaaaatggcatctgtgttct-3'	22	814	345
Probe	TET-5'-ctatgatcatccccatgctgaaccct-3'-TAMRA	26	839	346
Reverse	5'-tgaatgcattctggacttctct-3'	22	886	347

Table ABC. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag1730, Run 173761867	Tissue Name	Rel. Exp.(%) Ag1730, Run 173761867
Normal Colon	0.0	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	4.8	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0

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Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	5.3
Colon mets to lung (OD04451-01)	6.6	Normal Uterus	0.0
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	1.5
Ovarian Margin (OD06283-07)	0.0	Breast Cancer	6.7
Ovarian Cancer	**100.0**	Breast Cancer	17.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer	0.0	Breast Margin	0.0

		A2090734	
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	22.4
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	7.3
Lung Margin (OD05014B)	0.0	Normal Liver	6.7
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	15.7
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Cancer 6005-T	0.0
Liver Margin (ODO4310)	9.3	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer	0.0
Lung Margin (OD04321)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	28.1
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table ABD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1830, Run 165810392	Tissue Name	Rel. Exp.(%) Ag1830, Run 165810392
Secondary Th1 act	3.3	HUVEC IL-1beta	0.0
Secondary Th2 act	9.5	HUVEC IFN gamma	0.0

Secondary Tr1 act	2.1	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	3.9	Lung Microvascular EC none	13.6
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	9.2
Primary Th2 act	0.0	Microvascular Dermal EC none	44.4
Primary Tr1 act	2.2	Microsvasular Dermal EC TNFalpha + IL-1beta	11.2
Primary Th1 rest	9.5	Bronchial epithelium TNFalpha + IL1beta	4.2
Primary Th2 rest	2.4	Small airway epithelium none	3.5
Primary Tr1 rest	0.7	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	2.9	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	4.6	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	5.3	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	5.5	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	4.7	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	5.2	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	3.8	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	3.3
LAK cells IL-2	11.3	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	3.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	8.7	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	10.7	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	9.2	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	18.6	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0

Two Way MLR 7 day	4.4	HPAEC TNF alpha + IL-1 beta	3.5
PBMC rest	3.5	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	16.6
PBMC PHA-L	4.7	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	3.8
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	2.9	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	5.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	7.8
EOL-1 dbcAMP PMA/ionomycin	21.9	Dermal fibroblast CCD1070 IL-1 beta	3.3
Dendritic cells none	3.9	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	8.6	Dermal fibroblast IL-4	3.9
Dendritic cells anti-CD40	4.1	IBD Colitis 2	36.6
Monocytes rest	0.0	IBD Crohn's	2.5
Monocytes LPS	9.8	Colon	6.3
Macrophages rest	0.0	Lung	2.5
Macrophages LPS	0.0	Thymus	4.2
HUVEC none	0.0	Kidney	9.9
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1730 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag1730 Significant expression of the GMAP002345_A gene is seen exclusively in an ovarian cancer sample (CT = 33.1). Therefore, expression of this gene may be used to distinguish ovarian cancers from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of ovarian cancer.

Panel 4D Summary: Ag1830 Highest expression of the GMAP002345_A gene is seen in liver cirrhosis (CT=32.7). Furthermore, no expression in normal liver is seen in Panel 1.3D,

suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

Low but significant expression is also seen in a sample derived from a patient with IBD colitis, but not in normal colon. This observation suggests that the protein encoded by this gene may be involved in the inflammatory bowel disease process. Therefore, therapeutic modulation of the expression or function of this gene product could potentially be useful in treating the symptoms of this disease. Ag1730 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

AC. GMAP001524_B: GPCR

Expression of gene GMAP001524_B was assessed using the primer-probe sets Ag2226, Ag2384 and Ag1828, described in Tables ACA, ACB and ACC. Results of the RTQ-PCR runs are shown in Tables ACD and ACE.

Table ACA. Probe Name Ag2226

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggaaagtgtcctccctgttcta-3'	22	857	348
Probe	TET-5'-ccataatagtccccgtgttaaaccca-3'-TAMRA	26	881	349
Reverse	5'-ctttgacatccttgttcctcaa-3'	22	919	350

Table ACB. Probe Name Ag2384

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggaaagtgtcctccctgttcta-3'	22	857	351
Probe	TET-5'-ccataatagtccccgtgttaaaccca-3'-TAMRA	26	881	352
Reverse	5'-ctttgacatccttgttcctcaa-3'	22	919	353

Table ACC. Probe Name Ag1828

Primers	Sequences	Length	Start Position	SEQ ID NO:

Forward	5'-cctctccagcattctacacaac-3'	22	708	354
Probe	TET-5'-tctacagaaggcaggtccaaagcctt-3'-TAMRA	26	733	355
Reverse	5'-caattatgtgggaactgcaagt-3'	22	763	356

Table ACD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2384, Run 165629298	Tissue Name	Rel. Exp.(%) Ag2384, Run 165629298
Liver adenocarcinoma	10.5	Kidney (fetal)	9.5
Pancreas	1.3	Renal ca. 786-0	2.9
Pancreatic ca. CAPAN 2	3.7	Renal ca. A498	5.0
Adrenal gland	5.8	Renal ca. RXF 393	8.6
Thyroid	23.7	Renal ca. ACHN	6.1
Salivary gland	4.6	Renal ca. UO-31	2.3
Pituitary gland	5.6	Renal ca. TK-10	1.9
Brain (fetal)	7.6	Liver	1.3
Brain (whole)	2.4	Liver (fetal)	5.3
Brain (amygdala)	7.6	Liver ca. (hepatoblast) HepG2	0.1
Brain (cerebellum)	1.1	Lung	17.9
Brain (hippocampus)	6.2	Lung (fetal)	15.0
Brain (substantia nigra)	2.8	Lung ca. (small cell) LX-1	2.3
Brain (thalamus)	4.8	Lung ca. (small cell) NCI-H69	0.1
Cerebral Cortex	2.8	Lung ca. (s.cell var.) SHP-77	5.8
Spinal cord	13.9	Lung ca. (large cell)NCI-H460	4.8
glio/astro U87-MG	1.5	Lung ca. (non-sm. cell) A549	1.5
glio/astro U-118-MG	4.2	Lung ca. (non-s.cell) NCI-H23	3.1
astrocytoma SW1783	0.1	Lung ca. (non-s.cell) HOP-62	3.9
neuro*; met SK-N-AS	4.0	Lung ca. (non-s.cl) NCI-H522	1.8
astrocytoma SF-539	3.5	Lung ca. (squam.) SW 900	9.3
astrocytoma SNB-75	12.1	Lung ca. (squam.) NCI-H596	0.0
Glioma SNB-19	8.3	Mammary gland	15.4

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Glioma U251	3.8	Breast ca.* (pl.ef) MCF-7	7.1
Glioma SF-295	5.2	Breast ca.* (pl.ef) MDA-MB-231	12.5
Heart (Fetal)	15.5	Breast ca.* (pl. ef) T47D	1.8
Heart	20.6	Breast ca. BT-549	2.4
Skeletal muscle (Fetal)	8.0	Breast ca. MDA-N	0.7
Skeletal muscle	13.2	Ovary	51.8
Bone marrow	1.1	Ovarian ca. OVCAR-3	0.7
Thymus	2.2	Ovarian ca. OVCAR-4	4.4
Spleen	11.0	Ovarian ca. OVCAR-5	4.4
Lymph node	21.3	Ovarian ca. OVCAR-8	0.6
Colorectal	5.4	Ovarian ca. IGROV-1	0.6
Stomach	19.2	Ovarian ca. (ascites) SK-OV-3	1.2
Small intestine	60.7	Uterus	**100.0**
Colon ca. SW480	0.6	Placenta	4.5
Colon ca.* SW620 (SW480 met)	0.4	Prostate	8.1
Colon ca. HT29	0.3	Prostate ca.* (bone met) PC-3	3.2
Colon ca. HCT-116	5.3	Testis	17.9
Colon ca. CaCo-2	1.3	Melanoma Hs688(A).T	0.6
CC Well to Mod Diff (ODO3866)	2.5	Melanoma* (met) Hs688(B).T	0.2
Colon ca. HCC-2998	2.7	Melanoma UACC-62	0.9
Gastric ca. (liver met) NCI-N87	6.4	Melanoma M14	5.3
Bladder	2.5	Melanoma LOX IMVI	1.6
Trachea	24.5	Melanoma* (met) SK-MEL-5	1.8
Kidney	2.2	Adipose	7.2

Table ACE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1828, Run 165810353	Rel. Exp.(%) Ag2384, Run 162321123	Tissue Name	Rel. Exp.(%) Ag1828, Run 165810353	Rel. Exp.(%) Ag2384, Run 162321123
Secondary Th1 act	0.0	10.9	HUVEC IL-1beta	0.0	4.8
Secondary Th2 act	0.0	14.7	HUVEC IFN gamma	0.0	15.6
Secondary Tr1 act	0.0	11.6	HUVEC TNF alpha + IFN gamma	0.0	23.8
Secondary Th1 rest	0.0	6.6	HUVEC TNF alpha + IL4	0.0	24.8
Secondary Th2 rest	0.0	12.9	HUVEC IL-11	0.0	14.0
Secondary Tr1 rest	0.0	8.4	Lung Microvascular EC none	0.0	27.9
Primary Th1 act	0.0	8.2	Lung Microvascular EC TNFalpha + IL-1beta	0.0	17.7
Primary Th2 act	0.0	20.3	Microvascular Dermal EC none	0.0	22.1
Primary Tr1 act	22.7	17.4	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	15.8
Primary Th1 rest	0.0	22.7	Bronchial epithelium TNFalpha + IL1beta	0.0	17.4
Primary Th2 rest	3.5	16.0	Small airway epithelium none	0.0	7.3
Primary Tr1 rest	0.0	15.8	Small airway epithelium TNFalpha + IL-1beta	0.0	34.6
CD45RA CD4 lymphocyte act	0.0	19.3	Coronery artery SMC rest	0.0	81.8
CD45RO CD4 lymphocyte act	0.0	8.8	Coronery artery SMC TNFalpha + IL-1beta	0.0	41.8
CD8 lymphocyte act	0.0	9.0	Astrocytes rest	0.0	34.2
Secondary CD8	0.0	7.9	Astrocytes	0.0	26.1

lymphocyte rest			TNFalpha + IL-1beta		
Secondary CD8 lymphocyte act	0.0	11.2	KU-812 (Basophil) rest	0.0	13.7
CD4 lymphocyte none	0.0	9.2	KU-812 (Basophil) PMA/ionomycin	6.9	35.6
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	14.8	CCD1106 (Keratinocytes) none	0.0	19.3
LAK cells rest	0.0	16.8	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	23.7
LAK cells IL-2	0.0	5.1	Liver cirrhosis	**100.0**	4.1
LAK cells IL-2+IL-12	0.0	8.1	Lupus kidney	0.0	3.0
LAK cells IL-2+IFN gamma	0.0	9.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+IL-18	0.0	8.7	NCI-H292 IL-4	0.0	0.0
LAK cells PMA/ionomycin	0.0	27.5	NCI-H292 IL-9	0.0	0.0
NK Cells IL-2 rest	0.0	6.9	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	6.6	NCI-H292 IFN gamma	0.0	0.0
Two Way MLR 5 day	0.0	7.1	HPAEC none	0.0	9.7
Two Way MLR 7 day	0.0	6.2	HPAEC TNF alpha + IL-1 beta	0.0	13.2
PBMC rest	0.0	21.2	Lung fibroblast none	0.0	23.5
PBMC PWM	0.0	10.7	Lung fibroblast TNF alpha + IL-1 beta	0.0	6.8
PBMC PHA-L	0.0	15.0	Lung fibroblast IL-4	0.0	61.1
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	29.7
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	37.4
B lymphocytes PWM	0.0	17.6	Lung fibroblast IFN gamma	0.0	64.2
B lymphocytes	3.8	2.3	Dermal fibroblast	0.0	**100.0**

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CD40L and IL-4			CCD1070 rest		
EOL-1 dbcAMP	0.0	20.3	Dermal fibroblast CCD1070 TNF alpha	0.0	78.5
EOL-1 dbcAMP PMA/ionomycin	0.0	4.5	Dermal fibroblast CCD1070 IL-1 beta	0.0	54.0
Dendritic cells none	0.0	16.3	Dermal fibroblast IFN gamma	0.0	26.4
Dendritic cells LPS	0.0	21.5	Dermal fibroblast IL-4	0.0	42.0
Dendritic cells anti-CD40	7.6	24.1	IBD Colitis 2	8.1	4.3
Monocytes rest	0.0	44.8	IBD Crohn's	9.2	6.3
Monocytes LPS	0.0	3.4	Colon	31.9	30.4
Macrophages rest	3.7	34.2	Lung	3.8	33.0
Macrophages LPS	0.0	12.7	Thymus	0.0	4.0
HUVEC none	0.0	19.5	Kidney	0.0	16.8
HUVEC starved	0.0	25.5			

CNS_neurodegeneration_v1.0 Summary: Ag2226/Ag2384 Expression of this gene is low/undetectable (CTs > 35) across all of the samples in this panel (data not shown).

Panel 1.3D Summary: Ag2384 Highest expression of the GMAP001524_B gene is detected in the uterus (CT=28.8). There is also substantial expression in normal ovarian and small intestine tissue. Thus, the expression of this gene could be used to distinguish uterine, ovarian and small intestine tissue from other tissues in the panel. Of note is the low level of expression in cell lines derived from ovarian cancer. Therefore, the expression of this gene could be used to distinguish normal ovarian tissue from samples derived from ovarian cancer cell lines. Furthermore, therapeutic modulation of this gene or its protein product, through the use of small molecule drugs, antibodies or protein therapeutics may be beneficial in the treatment of ovarian cancer.

This gene is also moderately expressed (CT values = 31-33) in a variety of metabolic tissues, including adrenal, thyroid, pituitary, adult and fetal heart, adult and fetal skeletal muscle, fetal liver and adipose. Thus, this gene product may be a small molecule target for the treatment of metabolic disease, including obesity and Types 1 and 2 diabetes.

This gene is expressed at low to moderate levels in all CNS regions examined. The encoded protein is a novel member of the GPCR family of receptors. Several neurotransmitter receptors are GPCRs, including the dopamine receptor family, the serotonin receptor family, the GABAB receptor, muscarinic acetylcholine receptors, and others; thus, this GPCR may represent a novel neurotransmitter receptor. Targeting various neurotransmitter receptors (dopamine, serotonin) has proven to be an effective therapy in psychiatric illnesses such as schizophrenia, bipolar disorder and depression. In addition, other regions where this gene is expressed (the cerebral cortex and hippocampus) are known to play critical roles in Alzheimer's disease, seizure disorders, and in the normal process of memory formation. Thus, therapeutic modulation of the expression of this gene or its protein product may be beneficial in one or more of these diseases, as may blockade of the receptor encoded by the gene. Furthermore, significant levels of expression of this gene in areas outside the central nervous system (such as uterus and ovary), suggest the possibility of a wider role in intercellular signaling.

Ag2226 Expression of this gene is low/undetectable (CTs > 35) across all of the samples in this panel (data not shown).

Panel 2.2 Summary: Ag2226 Expression of this gene is low/undetectable (CTs > 35) across all of the samples in this panel (data not shown).

Panel 4D Summary: Ag2384 The GMAP001524_B transcript is expressed in most tissues in this panel regardless of treatment. This transcript encodes a GPCR like molecule with potential signaling activity that may be important in maintaining normal cellular functions in a number of tissues. Therapies designed with the protein encoded by this transcript could be important in regulating cellular viability or function. A second experiment with the probe and primer set Ag1828 is not consistent with the results with Ag2384 and shows low levels of transcript expression in liver cirrhosis only.

AD. GMAC040925_A: GPCR

Expression of gene GMAC040925_A was assessed using the primer-probe set Ag1824, described in Table ADA. Results of the RTQ-PCR runs are shown in Tables ADB and ADC.

Table ADA. Probe Name Ag1824

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ctcaatgtcctctcgtttcttg-3'	22	208	357
Probe	TET-5'-ttctgtggtcacacctaagctcttgg-3'-TAMRA	26	243	358
Reverse	5'-cttgtcagagaccaggaagttg-3'	22	270	359

Table ADB. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag1824, Run 213323519	Tissue Name	Rel. Exp.(%) Ag1824, Run 213323519
Adipose	5.2	Renal ca. TK-10	31.0
Melanoma* Hs688(A).T	0.0	Bladder	**100.0**
Melanoma* Hs688(B).T	0.9	Gastric ca. (liver met.) NCI-N87	62.0
Melanoma* M14	1.6	Gastric ca. KATO III	3.7
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	2.1
Melanoma* SK-MEL-5	3.5	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.6
Testis Pool	2.8	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	27.4
Prostate Pool	0.9	Colon ca. CaCo-2	4.5
Placenta	3.0	Colon cancer tissue	5.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	3.2	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	54.7	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	1.3	Colon Pool	1.5
Ovarian ca. OVCAR-5	40.3	Small Intestine Pool	0.0
Ovarian ca. IGROV-1	43.8	Stomach Pool	0.7
Ovarian ca. OVCAR-8	3.2	Bone Marrow Pool	3.0
Ovary	1.7	Fetal Heart	3.4

Breast ca. MCF-7	0.0	Heart Pool	1.0
Breast ca. MDA-MB-231	9.3	Lymph Node Pool	0.6
Breast ca. BT 549	9.4	Fetal Skeletal Muscle	0.0
Breast ca. T47D	24.1	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	1.8	Spleen Pool	4.9
Breast Pool	1.0	Thymus Pool	9.1
Trachea	12.1	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.0	CNS cancer (glio/astro) U-118-MG	9.3
Fetal Lung	36.6	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	1.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	0.0	CNS cancer (glio) SNB-19	57.8
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	0.0
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	31.0	Brain (fetal)	3.0
Lung ca. NCI-H460	11.7	Brain (Hippocampus) Pool	3.0
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	0.0
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	0.0
Liver	0.0	Brain (Thalamus) Pool	2.8
Fetal Liver	0.0	Brain (whole)	6.0
Liver ca. HepG2	2.8	Spinal Cord Pool	0.0
Kidney Pool	6.1	Adrenal Gland	0.0
Fetal Kidney	0.0	Pituitary gland Pool	0.0
Renal ca. 786-0	2.8	Salivary Gland	0.0
Renal ca. A498	41.5	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	42.0
Renal ca. UO-31	0.8	Pancreas Pool	13.1

Table ADC. Panel 4D

Tissue Name	Rel. Exp.(%)	Tissue Name	Rel. Exp.(%)

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	Ag1824, Run 165809019		Ag1824, Run 165809019
Secondary Th1 act	0.0	HUVEC IL-1beta	1.8
Secondary Th2 act	0.0	HUVEC IFN gamma	7.3
Secondary Tr1 act	0.7	HUVEC TNF alpha + IFN gamma	1.9
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	4.7
Secondary Tr1 rest	0.0	Lung Microvascular EC none	28.9
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	7.0
Primary Th2 act	1.4	Microvascular Dermal EC none	7.2
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	1.1
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	15.0
Primary Th2 rest	0.0	Small airway epithelium none	18.2
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	**100.0**
CD45RA CD4 lymphocyte act	0.4	Coronery artery SMC rest	1.3
CD45RO CD4 lymphocyte act	0.5	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	11.9
Secondary CD8 lymphocyte rest	1.3	Astrocytes TNFalpha + IL-1beta	58.2
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	1.4
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	3.2
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.7	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	19.1
LAK cells IL-2	0.7	Liver cirrhosis	21.3
LAK cells IL-2+IL-12	0.0	Lupus kidney	2.6
LAK cells IL-2+IFN gamma	0.6	NCI-H292 none	7.9
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	17.0
LAK cells	0.0	NCI-H292 IL-9	5.0

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PMA/ionomycin			
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	10.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.4
Two Way MLR 5 day	0.0	HPAEC none	2.3
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	1.3
PBMC rest	0.0	Lung fibroblast none	2.0
PBMC PWM	0.2	Lung fibroblast TNF alpha + IL-1 beta	0.3
PBMC PHA-L	0.0	Lung fibroblast IL-4	5.8
Ramos (B cell) none	0.0	Lung fibroblast IL-9	4.5
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.4
B lymphocytes PWM	0.3	Lung fibroblast IFN gamma	2.0
B lymphocytes CD40L and IL-4	1.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.9
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.5
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	1.1
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.2	IBD Colitis 2	11.4
Monocytes rest	0.0	IBD Crohn's	12.0
Monocytes LPS	0.9	Colon	14.5
Macrophages rest	0.0	Lung	3.7
Macrophages LPS	0.0	Thymus	2.9
HUVEC none	2.7	Kidney	0.0
HUVEC starved	4.6		

General_screening_panel_v1.4 Summary: Ag1824 Expression of the GMAP001260_A gene is highest in a sample derived from normal bladder tissue (CT = 32.6). In addition, it appears to be expressed by several cell lines derived from pancreatic cancer, glioma, colon cancer, gastric cancer, renal cancer, lung cancer, ovarian cancer and breast cancer. Thus, the expression of this gene could be used to distinguish normal bladder tissue from the other samples in the panel. Moreover, therapeutic modulation of this gene or its protein product, through the use of antibodies, small molecule drugs or protein therapeutics might be of

benefit in the treatment of pancreatic cancer, glioma, colon cancer, gastric cancer, renal cancer, lung cancer, ovarian cancer or breast cancer.

Panel 4D Summary: <u>Ag1824</u> Expression of the GMAC040925_A gene is significantly up-regulated (5 fold) in small airway epithelium treated with the pro-inflammatory cytokines Il-1b and TNFα and to a certain degree on astrocytes treated with TNF-α + IL-1b. In addition, moderate constitutive expression (CT = 31.1) is found in lung microvascular endothelial cells. Therefore, therapeutic modulation of the GMAC040925_A gene with monoclonal antibodies or small molecule therapeutics might be relevant for the treatment of asthma.

AE. GMAL160314_A: GPCR

Expression of gene GMAL160314_A was assessed using the primer-probe sets Ag1795 and Ag1822, described in Tables AEA and AEB. Results of the RTQ-PCR runs are shown in Table AEC.

<u>Table AEA</u>. Probe Name Ag1795

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-catcattcctagtggcatcact-3'	22	745	360
Probe	TET-5'-tgactccctcccagaaagaatatctgg-3'-TAMRA	27	780	361
Reverse	5'-accaaagggatcttgttgatct-3'	22	807	362

<u>Table AEB</u>. Probe Name Ag1822

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-catcattcctagtggcatcact-3'	22	745	363
Probe	TET-5'-tgactccctcccagaaagaatatctgg-3'-TAMRA	27	780	364
Reverse	5'-accaaagggatcttgttgatct-3'	22	807	365

<u>Table AEC</u>. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1795, Run 165810587	Rel. Exp.(%) Ag1822, Run 165808999	Tissue Name	Rel. Exp.(%) Ag1795, Run 165810587	Rel. Exp.(%) Ag1822, Run 165808999

Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	0.0	0.6
Secondary Tr1 act	0.0	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	1.1
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	0.8
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	1.2	Microsvasular Dermal EC TNFalpha + IL-1beta	2.7	0.0
Primary Th1 rest	0.0	0.7	Bronchial epithelium TNFalpha + IL1beta	3.0	1.2
Primary Th2 rest	4.3	0.0	Small airway epithelium none	0.0	0.9
Primary Tr1 rest	0.0	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0	2.5
CD45RA CD4 lymphocyte act	0.0	0.0	Coronery artery SMC rest	3.7	0.0
CD45RO CD4 lymphocyte act	2.3	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8 lymphocyte rest	0.0	0.7	Astrocytes TNFalpha + IL-1beta	0.0	0.8
Secondary CD8 lymphocyte act	0.0	0.0	KU-812 (Basophil) rest	0.0	1.2
CD4 lymphocyte	0.0	0.0	KU-812	2.6	0.0

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none			(Basophil) PMA/ionomycin		
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	0.0	0.0	Liver cirrhosis	32.5	32.8
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	0.0	4.1
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+IL-18	4.6	1.6	NCI-H292 IL-4	0.0	4.3
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	6.3	0.9
NK Cells IL-2 rest	0.0	0.0	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	0.0	NCI-H292 IFN gamma	0.0	1.2
Two Way MLR 5 day	0.0	0.0	HPAEC none	0.0	1.9
Two Way MLR 7 day	0.0	1.0	HPAEC TNF alpha + IL-1 beta	0.0	0.0
PBMC rest	0.0	0.0	Lung fibroblast none	0.0	0.0
PBMC PWM	0.0	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	1.9
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	1.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	2.5	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.8
B lymphocytes CD40L and IL-4	2.8	1.1	Dermal fibroblast CCD1070 rest	0.0	0.0
EOL-1 dbcAMP	0.0	2.1	Dermal fibroblast CCD1070 TNF alpha	0.0	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast	0.0	1.1

PMA/ionomycin			CCD1070 IL-1 beta		
Dendritic cells none	0.0	0.0	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.0	0.0
Dendritic cells anti-CD40	0.0	1.6	IBD Colitis 2	4.8	5.9
Monocytes rest	0.0	0.0	IBD Crohn's	0.0	1.0
Monocytes LPS	0.0	0.0	Colon	**100.0**	**100.0**
Macrophages rest	0.0	0.0	Lung	8.8	5.2
Macrophages LPS	0.0	1.1	Thymus	4.8	6.4
HUVEC none	0.0	0.0	Kidney	0.0	0.0
HUVEC starved	3.8	0.0			

Panel 1.3D Summary: <u>Ag1795</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: <u>Ag1795</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5 **Panel 4D Summary:** <u>Ag1795/Ag1822</u> Results from two experiments using identical probe/primer sets are in good agreement. Low but significant expression of the GMAL160314_A gene is detected exclusively in colon. Therefore, expression of this gene may be used to distinguish colon from the other samples on this panel. Furthermore, expression of this gene is decreased in colon samples from patients with IBD colitis and 10 Crohn's disease relative to normal colon. Therefore, therapeutic modulation of the activity of the GPCR encoded by this gene, using small molecule drugs, antibodies or protein therapeutics, may be useful in the treatment of inflammatory bowel disease.

AF. GMAP002509_B/CG149867-01: Olfactory Receptor

15 Expression of gene GMAP002509_B (also known as CG149867-01) was assessed using the primer-probe set Ag1792, described in Table AFA. Results of the RTQ-PCR runs are shown in Tables AFB and AFC.

<u>Table AFA</u>. Probe Name Ag1792

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Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gtgggttcatatgcctgttaaa-3'	22	625	366
Probe	TET-5'-tcttgctcctggtctcctatatggtca-3'-TAMRA	27	652	367
Reverse	5'-gctgtgggtccttaaggagtac-3'	22	683	368

Table AFB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1792, Run 165974810	Tissue Name	Rel. Exp.(%) Ag1792, Run 165974810
Liver adenocarcinoma	11.3	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	3.8
Adrenal gland	0.0	Renal ca. RXF 393	21.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	23.3
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	25.9
Brain (cerebellum)	0.0	Lung	13.6
Brain (hippocampus)	0.0	Lung (fetal)	42.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
Glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
Glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	1.3
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	3.3
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0

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astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	25.7
Skeletal muscle (fetal)	5.1	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	4.5
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	20.6
Small intestine	1.1	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	2.2
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0

Kidney	0.0	Adipose	0.0

Table AFC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1792, Run 165811472	Tissue Name	Rel. Exp.(%) Ag1792, Run 165811472
Secondary Th1 act	0.0	HUVEC IL-1beta	3.5
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	3.6	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0

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LAK cells IL-2+IFN gamma	0.8	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.3
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	7.5	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	1.7	Dermal fibroblast CCD1070 IL-1 beta	5.3
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	9.1	IBD Colitis 2	24.3
Monocytes rest	0.0	IBD Crohn's	7.3
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	4.2
Macrophages LPS	0.0	Thymus	3.8
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1792 Expression of the GMAP002509_B gene is highest in spleen (CT = 33.1), an important site of secondary immune responses. Therefore, expression of this gene may be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune

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diseases, and inflammatory diseases. This gene is also expressed at low but significant levels in fetal lung.

Panel 2.2 Summary: Ag1792 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5   **Panel 4D Summary:** Ag1792: Expression of the GMAP002509_B gene is detected in a liver cirrhosis sample (CT = 31.53). This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis. Low level expression of this transcript was also detected in an IBD colitis tissue sample (CT=33.6) and thus may be involved in inflammatory bowel diseases.

AG. GMAP002407_A: GPCR

Expression of gene GMAP002407_A was assessed using the primer-probe sets Ag2696 and Ag1790, described in Tables AGA and AGB. Results of the RTQ-PCR runs are
15   shown in Tables AGC, AGD and AGE.

Table AGA. Probe Name Ag2696

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-actacgtgccacctgtctgtat-3'	22	797	369
Probe	TET-5'-ctacctgcagcctcgctccagtgag-3'-TAMRA	25	819	370
Reverse	5'-agcattggagttacgattgtgt-3'	22	872	371

Table AGB. Probe Name Ag1790

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cctgtacacagtcatggcctat-3'	22	384	372
Probe	TET-5'-atctgtcaacccctgcactacccagt-3'-TAMRA	26	421	373
Reverse	5'-atttctgcacacatccttctgt-3'	22	455	374

Table AGC. Panel 1.3D

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Tissue Name	Rel. Exp.(%) Ag1790, Run 165974809	Tissue Name	Rel. Exp.(%) Ag1790, Run 165974809
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	8.7	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	54.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	3.7	Liver (fetal)	0.0
Brain (amygdala)	10.6	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	6.8	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
Glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
Glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef)	0.0

		T47D	
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	20.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	7.6
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	6.1	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table AGD. Panel 2D

Tissue Name	Rel. Exp.(%) Ag2696, Run 153291452	Tissue Name	Rel. Exp.(%) Ag2696, Run 153291452
Normal Colon	21.6	Kidney Margin 8120608	0.0

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CC Well to Mod Diff (ODO3866)	10.2	Kidney Cancer 8120613	0.0
CC Margin (ODO3866)	19.2	Kidney Margin 8120614	0.0
CC Gr.2 rectosigmoid (ODO3868)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3868)	0.0	Kidney Margin 9010321	0.0
CC Mod Diff (ODO3920)	12.9	Normal Uterus	0.0
CC Margin (ODO3920)	10.4	Uterus Cancer 064011	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Normal Thyroid	0.0
CC Margin (ODO3921)	0.0	Thyroid Cancer 064010	0.0
CC from Partial Hepatectomy (ODO4309) Mets	0.0	Thyroid Cancer A302152	0.0
Liver Margin (ODO4309)	0.0	Thyroid Margin A302153	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Breast	0.0
Lung Margin (OD04451-02)	0.0	Breast Cancer (OD04566)	0.0
Normal Prostate 6546-1	0.0	Breast Cancer (OD04590-01)	0.0
Prostate Cancer (OD04410)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Prostate Margin (OD04410)	0.0	Breast Cancer Metastasis (OD04655-05)	0.0
Prostate Cancer (OD04720-01)	0.0	Breast Cancer 064006	0.0
Prostate Margin (OD04720-02)	0.0	Breast Cancer 1024	6.9
Normal Lung 061010	14.2	Breast Cancer 9100266	0.0
Lung Met to Muscle (ODO4286)	0.0	Breast Margin 9100265	0.0
Muscle Margin (ODO4286)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0

Lung Margin (OD03126)	0.0	Normal Liver	0.0
Lung Cancer (OD04404)	**100.0**	Liver Cancer 064003	0.0
Lung Margin (OD04404)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04565)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD04565)	0.0	Liver Cancer 6004-T	0.0
Lung Cancer (OD04237-01)	0.0	Liver Tissue 6004-N	0.0
Lung Margin (OD04237-02)	0.0	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	0.0	Normal Bladder	43.2
Melanoma Mets to Lung (OD04321)	0.0	Bladder Cancer 1023	0.0
Lung Margin (OD04321)	0.0	Bladder Cancer A302173	0.0
Normal Kidney	8.8	Bladder Cancer (OD04718-01)	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Normal Adjacent (OD04718-03)	13.2
Kidney Margin (OD04338)	0.0	Normal Ovary	0.0
Kidney Ca Nuclear grade ½ (OD04339)	0.0	Ovarian Cancer 064008	0.0
Kidney Margin (OD04339)	0.0	Ovarian Cancer (OD04768-07)	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Ovary Margin (OD04768-08)	0.0
Kidney Margin (OD04340)	14.2	Normal Stomach	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 9060358	0.0
Kidney Margin (OD04348)	0.0	Stomach Margin 9060359	11.3
Kidney Cancer (OD04622-01)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04622-03)	0.0	Stomach Margin 9060394	0.0
Kidney Cancer (OD04450-01)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04450-03)	2.3	Stomach Margin 9060396	12.4

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Kidney Cancer 8120607	0.0	Gastric Cancer 064005	0.0

Table AGE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1790, Run 165801864	Tissue Name	Rel. Exp.(%) Ag1790, Run 165801864
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	1.8	HUVEC TNF alpha + IL4	7.5
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	5.7
Primary Th2 rest	0.0	Small airway epithelium none	3.9
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	56.3
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	10.0
CD8 lymphocyte act	0.0	Astrocytes rest	4.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	3.8
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	36.6
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**

LAK cells IL-2+IL-12	0.0	Lupus kidney	8.8
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	2.6
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	65.1
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	5.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	3.7	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	3.4
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	5.7
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	6.0
Macrophages rest	0.0	Lung	8.1
Macrophages LPS	0.0	Thymus	20.7
HUVEC none	0.0	Kidney	8.5
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag2696 Expression of this gene is low/undetectable (CT>35) in all of the samples in this panel (data not shown).

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Panel 1.3D Summary: Ag1790 The GMAP002407_A gene is only expressed at detectable levels in the spleen (CT=33.9), an important site of secondary immune responses. Therefore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: Ag1790 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2D Summary: Ag2696 Expression of the GMAP002407_A gene is restricted to a lung cancer sample (CT=34.3). This gene appears to be overexpressed in lung cancer when compared to adjacent normal tissue. Therefore, expression of this gene could be used to as a marker for lung cancer. Furthermore, therapeutic modulation of the expression or function of the protein product, using small molecule drugs or antibodies, may be effective in the treatment of lung cancer.

Panel 4D Summary: Ag1790 The GMAP002407_A gene is expressed at highest levels in small airway epithelium (CT=33.5). Therefore, expression of this gene could be used to distinguish small airway epithelium from the other samples on this panel. Furthermore, antibodies or small molecule drugs that inhibit the action of the GMAP002407_A gene product may reduce or eliminate the symptoms in patients with asthma, allergies, and chronic obstructive pulmonary disease. Ag2696 Expression of this gene is low/undetectable (CT>35) in all of the samples in this panel (data not shown).

AH. GMAL391156_B and GMAC024399_B: GPCR

Expression of gene GMAL391156_B and variant GMAC024399_B was assessed using the primer-probe sets Ag1788, Ag1717, and Ag1715, described in Tables AHA, AHB and AHC. Results of the RTQ-PCR runs are shown in Tables AHD and AHE.

Table AHA. Probe Name Ag1788

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atcttcctcgagtcaccaaact-3'	22	548	375

Probe	TET-5'-tgcctgcctggactcttacatcattg-3'-TAMRA	26	570	376
Reverse	5'-agtgcttagggaaagaattcca-3'	22	618	377

Table AHB. Probe Name Ag1717

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atcttcctcgagtcaccaaact-3'	22	548	378
Probe	TET-5'-tgcctgcctggactcttacatcattg-3'-TAMRA	26	570	379
Reverse	5'-agtgcttagggaaagaattcca-3'	22	618	380

Table AHC. Probe Name Ag1715

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atcttcctcgagtcaccaaact-3'	22	548	381
Probe	TET-5'-tgcctgcctggactcttacatcattg-3'-TAMRA	26	570	382
Reverse	5'-agtgcttagggaaagaattcca-3'	22	618	383

Table AHD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1788, Run 165974808	Tissue Name	Rel. Exp.(%) Ag1788, Run 165974808
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.)	0.0

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		SHP-77	
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
Glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
Glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	6.9
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	1.6	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	2.4	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	27.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0

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Colon ca. HCT-116	0.0		Testis	0.0	
Colon ca. CaCo-2	0.0		Melanoma Hs688(A).T	0.0	
Colon ca. tissue(ODO3866)	0.0		Melanoma* (met) Hs688(B).T	0.0	
Colon ca. HCC-2998	0.0		Melanoma UACC-62	0.0	
Gastric ca.* (liver met) NCI-N87	0.0		Melanoma M14	0.0	
Bladder	0.0		Melanoma LOX IMVI	0.0	
Trachea	0.0		Melanoma* (met) SK-MEL-5	0.0	
Kidney	0.0		Adipose	0.0	

Table AHE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1717, Run 165767645	Rel. Exp.(%) Ag1788, Run 165801807	Tissue Name	Rel. Exp.(%) Ag1717, Run 165767645	Rel. Exp.(%) Ag1788, Run 165801807
Secondary Th1 act	2.5	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	0.0	0.0
Secondary Tr1 act	0.0	3.9	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0
Primary Th1 rest	0.0	0.0	Bronchial	0.0	0.0

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			epithelium TNFalpha + IL1beta		
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	0.0	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0	0.0
CD45RA CD4 lymphocyte act	0.0	0.0	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8 lymphocyte rest	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0
Secondary CD8 lymphocyte act	0.0	2.2	KU-812 (Basophil) rest	0.0	0.0
CD4 lymphocyte none	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	0.0	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	0.0	0.0	Liver cirrhosis	**100.0**	**100.0**
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	0.0	0.0
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+IL-18	0.0	0.0	NCI-H292 IL-4	0.0	0.0
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	0.0	0.0
NK Cells IL-2 rest	0.0	0.0	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	22.5	NCI-H292 IFN gamma	0.0	0.0
Two Way MLR 5 day	0.0	0.0	HPAEC none	0.0	0.0

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Two Way MLR 7 day	0.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	0.0
PBMC rest	0.0	0.0	Lung fibroblast none	0.0	0.0
PBMC PWM	0.0	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	4.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes CD40L and IL-4	0.0	0.0	Dermal fibroblast CCD1070 rest	0.0	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	2.6
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0
Dendritic cells none	0.0	0.0	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.0	0.0
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	49.3	54.0
Monocytes rest	0.0	0.0	IBD Crohn's	8.8	2.0
Monocytes LPS	0.0	0.0	Colon	0.0	3.5
Macrophages rest	0.0	0.0	Lung	0.0	9.2
Macrophages LPS	0.0	0.0	Thymus	0.0	0.0
HUVEC none	0.0	0.0	Kidney	0.0	0.0
HUVEC starved	0.0	0.0			

Panel 1.3D Summary: <u>Ag1788</u> The GMAL391156_B gene is expressed at detectable levels only in the spleen (CT = 33), an important site of secondary immune responses. Therefore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: <u>Ag1788</u> Expression of this gene is low/undetectable (CTs > 35) in all samples on this panel (data not shown).

Panel 4D Summary: <u>Ag1717/Ag1788</u> Results from two experiments using probe/primer sets of identical sequence are in good agreement. Highest expression of the GMAL391156_B gene is seen in liver cirrhosis (CT=32). Furthermore, no expression in normal liver is seen in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

Low but significant expression is also seen in a sample derived from a patient with IBD colitis (CT = 33), but not in normal colon. This observation suggests that the protein encoded by this gene may be involved in the inflammatory bowel disease process. Therefore, therapeutic modulation of the expression or function of this gene product could potentially be useful in treating the symptoms of this disease.

<u>Ag1715</u> Expression of this gene is low/undetectable (CTs > 35) in all samples on this panel (data not shown).

AI. GMAL356019_D: GPCR

Expression of gene GMAL356019_D was assessed using the primer-probe set Ag1785, described in Table AIA. Results of the RTQ-PCR runs are shown in Tables AIB and AIC.

<u>Table AIA</u>. Probe Name Ag1785

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tgtgcttaaggttccttcttca-3'	22	673	384
Probe	TET-5'-atggcaaaaggccatctctacctgtg-3'-TAMRA	26	700	385
Reverse	5'-atggctccatagaacagagaca-3'	22	744	386

<u>Table AIB</u>. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1785, Run	Tissue Name	Rel. Exp.(%) Ag1785, Run

	165941605		165941605
Liver adenocarcinoma	34.2	Kidney (fetal)	0.0
Pancreas	11.3	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	11.1	Renal ca. A498	7.3
Adrenal gland	5.3	Renal ca. RXF 393	30.6
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	11.8	Renal ca. UO-31	10.5
Pituitary gland	9.3	Renal ca. TK-10	0.0
Brain (fetal)	31.6	Liver	0.0
Brain (whole)	10.4	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	21.8
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	11.4
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
Glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	10.4
Glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	23.0
astrocytoma SW1783	18.8	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	9.1	Lung ca. (non-s.cl) NCI-H522	10.7
astrocytoma SF-539	5.0	Lung ca. (squam.) SW 900	11.6
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
Glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	8.3
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	29.5
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	19.6	Breast ca. BT-549	4.5

Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	2.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	81.2
Small intestine	8.4	Uterus	6.0
Colon ca. SW480	0.0	Plancenta	16.3
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	8.2
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	10.4
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	9.3
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	10.9
Bladder	11.7	Melanoma LOX IMVI	11.2
Trachea	3.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	11.0	Adipose	0.0

Table AIC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1785, Run 165809004	Tissue Name	Rel. Exp.(%) Ag1785, Run 165809004
Secondary Th1 act	6.7	HUVEC IL-1beta	0.0
Secondary Th2 act	7.6	HUVEC IFN gamma	10.6
Secondary Tr1 act	5.3	HUVEC TNF alpha + IFN gamma	0.0

Secondary Th1 rest	2.9	HUVEC TNF alpha + IL4	2.7
Secondary Th2 rest	4.4	HUVEC IL-11	0.0
Secondary Tr1 rest	11.0	Lung Microvascular EC none	9.5
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	20.3
Primary Th2 act	0.0	Microvascular Dermal EC none	11.2
Primary Tr1 act	3.1	Microsvasular Dermal EC TNFalpha + IL-1beta	12.1
Primary Th1 rest	8.2	Bronchial epithelium TNFalpha + IL1beta	2.3
Primary Th2 rest	3.1	Small airway epithelium none	11.4
Primary Tr1 rest	6.5	Small airway epithelium TNFalpha + IL-1beta	38.7
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	10.2	Coronery artery SMC TNFalpha + IL-1beta	2.4
CD8 lymphocyte act	5.6	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	11.0	Astrocytes TNFalpha + IL-1beta	10.1
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	3.8
CD4 lymphocyte none	33.0	KU-812 (Basophil) PMA/ionomycin	17.2
2ry Th1/Th2/Tr1_anti-CD95 CH11	13.0	CCD1106 (Keratinocytes) none	12.2
LAK cells rest	0.7	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	13.9
LAK cells IL-2	4.1	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	17.0	Lupus kidney	7.0
LAK cells IL-2+IFN gamma	27.2	NCI-H292 none	17.7
LAK cells IL-2+ IL-18	8.4	NCI-H292 IL-4	9.5
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	14.1
NK Cells IL-2 rest	15.9	NCI-H292 IL-13	5.5
Two Way MLR 3 day	7.0	NCI-H292 IFN gamma	9.7
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	6.3

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PBMC rest	0.0	Lung fibroblast none	15.5
PBMC PWM	6.7	Lung fibroblast TNF alpha + IL-1 beta	7.8
PBMC PHA-L	0.0	Lung fibroblast IL-4	10.2
Ramos (B cell) none	7.3	Lung fibroblast IL-9	15.3
Ramos (B cell) ionomycin	4.5	Lung fibroblast IL-13	11.6
B lymphocytes PWM	4.7	Lung fibroblast IFN gamma	20.7
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	8.5
EOL-1 dbcAMP	3.2	Dermal fibroblast CCD1070 TNF alpha	23.7
EOL-1 dbcAMP PMA/ionomycin	3.0	Dermal fibroblast CCD1070 IL-1 beta	3.7
Dendritic cells none	9.8	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	5.5	Dermal fibroblast IL-4	4.5
Dendritic cells anti-CD40	5.0	IBD Colitis 2	18.6
Monocytes rest	0.0	IBD Crohn's	11.9
Monocytes LPS	0.0	Colon	22.5
Macrophages rest	10.7	Lung	3.8
Macrophages LPS	0.0	Thymus	10.2
HUVEC none	6.1	Kidney	4.3
HUVEC starved	8.0		

Panel 1.3D Summary: Ag1785 Expression of the GMAL356019_D gene is highest in spleen (CT = 34.1), an important site of secondary immune responses. Therefore, expression of this gene can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases. This gene is also expressed at low but significant levels in an ovarian cancer cell line.

Panel 2.2 Summary: Ag1785 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1785 Expression of the GMAL356019_D gene is highest in a liver cirrhosis sample (CT = 31.9). Furthermore, no expression in normal liver is seen in Panel 1.3D,

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suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

5   This gene is also expressed at low levels in TNF-alpha+IL-1beta-stimulated small airway epithelium, resting CD4 T lymphocytes, IL-2+IFN-gamma-stimulated LAK cells, and TNF-alpha-stimulated CCD1070 dermal fibroblasts. Therefore, antibodies or small molecule drugs that inhibit the function of this gene product may reduce or eliminate the symptoms of patients with asthma, allergies, and psoriasis. In addition, the low-level expression in both

10   resting CD4 T lymphocytes and cytokine-stimulated LAK cells indicate that small molecule drugs that inhibit the function of the GPCR encoded by this gene may also reduce or eliminate the symptoms of patients with various T cell-dependent autoimmune and inflammatory diseases, such as, but not limited to, rheumatoid arthritis, inflammatory bowel diseases, and multiple sclerosis.

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AJ. GMAL163152_D AND GMAL356019_A: GPCR

Expression of gene GMAL163152_D and variant GMAL356019_A was assessed using the primer-probe sets Ag2484, Ag1781, Ag1783 and Ag1583, described in Tables AJA, AJB, AJC and AJD. Results of the RTQ-PCR runs are shown in Tables AJE and AJF.

20   Table AJA. Probe Name Ag2484

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggctacttgtacaatggaatgg-3'	22	467	387
Probe	TET-5'-caagccacagaaccaacgataatgca-3'-TAMRA	26	431	388
Reverse	5'-tcaaccatcatgaaccctagag-3'	22	402	389

Table AJB. Probe Name Ag1781

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gatgctcaacttctggtctttg-3'	22	69	390
Probe	TET-5'-catcctccctggaaatttcctcatca-3'-	26	116	391

	TAMRA			
Reverse	5'-cagggtctgactttatggtgaa-3'	22	144	392

Table AJC. Probe Name Ag1783

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gatgctcaacttctggtctttg-3'	22	69	393
Probe	TET-5'-catcctccctggaaatttcctcatca-3'-TAMRA	26	116	394
Reverse	5'-cagggtctgactttatggtgaa-3'	22	144	395

Table AJD. Probe Name Ag1583

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gatgctcaacttctggtctttg-3'	22	69	396
Probe	TET-5'-catcctccctggaaatttcctcatca-3'-TAMRA	26	116	397
Reverse	5'-cagggtctgactttatggtgaa-3'	22	144	398

Table AJE. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1781, Run 165941533	Rel. Exp.(%) Ag1783, Run 165941554	Tissue Name	Rel. Exp.(%) Ag1781, Run 165941533	Rel. Exp.(%) Ag1783, Run 165941554
Liver adenocarcinoma	2.0	0.0	Kidney (fetal)	0.0	0.0
Pancreas	0.0	0.0	Renal ca. 786-0	0.0	0.0
Pancreatic ca. CAPAN 2	0.0	0.0	Renal ca. A498	0.0	0.0
Adrenal gland	0.0	0.0	Renal ca. RXF 393	7.6	0.0
Thyroid	0.0	0.0	Renal ca. ACHN	0.0	0.0
Salivary gland	0.0	0.0	Renal ca. UO-31	0.0	0.0
Pituitary gland	0.0	0.0	Renal ca. TK-10	0.0	0.0
Brain (fetal)	0.0	0.0	Liver	0.0	0.0
Brain (whole)	0.0	0.0	Liver (fetal)	0.0	0.0
Brain (amygdala)	0.0	0.0	Liver ca. (hepatoblast) HepG2	0.0	0.0

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Brain (cerebellum)	0.0	0.0	Lung	0.0	0.0
Brain (hippocampus)	0.0	0.0	Lung (fetal)	0.0	0.0
Brain (substantia nigra)	0.0	0.0	Lung ca. (small cell) LX-1	0.0	0.0
Brain (thalamus)	0.0	0.0	Lung ca. (small cell) NCI-H69	0.0	0.0
Cerebral Cortex	0.0	0.0	Lung ca. (s.cell var.) SHP-77	0.0	0.0
Spinal cord	0.0	0.0	Lung ca. (large cell)NCI-H460	0.0	0.0
Glio/astro U87-MG	0.0	0.0	Lung ca. (non-sm. cell) A549	0.0	0.0
glio/astro U-118-MG	0.0	0.0	Lung ca. (non-s.cell) NCI-H23	0.0	0.0
astrocytoma SW1783	0.0	0.0	Lung ca. (non-s.cell) HOP-62	0.0	0.0
neuro*; met SK-N-AS	0.0	0.0	Lung ca. (non-s.cl) NCI-H522	0.0	0.0
astrocytoma SF-539	0.0	0.0	Lung ca. (squam.) SW 900	0.0	0.0
astrocytoma SNB-75	0.0	0.0	Lung ca. (squam.) NCI-H596	0.0	0.0
Glioma SNB-19	0.0	0.0	Mammary gland	0.0	0.0
Glioma U251	0.0	14.5	Breast ca.* (pl.ef) MCF-7	0.0	0.0
Glioma SF-295	0.0	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0	0.0
Heart (fetal)	0.0	0.0	Breast ca.* (pl.ef) T47D	0.0	0.0
Heart	0.0	0.0	Breast ca. BT-549	0.0	0.0
Skeletal muscle (fetal)	0.0	0.0	Breast ca. MDA-N	0.0	0.0

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Tissue Name	Rel. Exp.(%)	Rel. Exp.(%)	Tissue Name	Rel. Exp.(%)	Rel. Exp.(%)
Skeletal muscle	0.0	0.0	Ovary	0.0	0.0
Bone marrow	0.0	0.0	Ovarian ca. OVCAR-3	0.0	0.0
Thymus	0.0	0.0	Ovarian ca. OVCAR-4	0.0	0.0
Spleen	**100.0**	**100.0**	Ovarian ca. OVCAR-5	0.0	0.0
Lymph node	0.0	0.0	Ovarian ca. OVCAR-8	0.0	0.0
Colorectal	2.0	0.0	Ovarian ca. IGROV-1	0.0	0.0
Stomach	0.0	0.0	Ovarian ca.* (ascites) SK-OV-3	5.5	32.3
Small intestine	0.0	0.0	Uterus	0.0	0.0
Colon ca. SW480	0.0	0.0	Plancenta	0.0	0.0
Colon ca.* SW620(SW480 met)	0.0	0.0	Prostate	0.0	0.0
Colon ca. HT29	0.0	0.0	Prostate ca.* (bone met)PC-3	0.0	0.0
Colon ca. HCT-116	0.0	0.0	Testis	1.1	13.3
Colon ca. CaCo-2	0.0	0.0	Melanoma Hs688(A).T	0.0	0.0
Colon ca. tissue(ODO3866)	0.0	0.0	Melanoma* (met) Hs688(B).T	0.0	0.0
Colon ca. HCC-2998	0.0	0.0	Melanoma UACC-62	0.0	0.0
Gastric ca.* (liver met) NCI-N87	0.0	11.4	Melanoma M14	0.0	0.0
Bladder	0.0	0.0	Melanoma LOX IMVI	0.0	0.0
Trachea	0.0	0.0	Melanoma* (met) SK-MEL-5	0.0	0.0
Kidney	0.0	0.0	Adipose	0.0	0.0

Table AJF. Panel 4D

Tissue Name	Rel. Exp.(%)	Rel. Exp.(%)	Tissue Name	Rel. Exp.(%)	Rel. Exp.(%)

	Ag1781, Run 165806967	Ag1783, Run 165807017		Ag1781, Run 165806967	Ag1783, Run 165807017
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	0.0	0.0
Secondary Tr1 act	0.0	13.2	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0
Primary Th1 rest	0.0	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	0.0	0.0	Small airway epithelium TNFalpha + IL-1beta	3.0	0.0
CD45RA CD4 lymphocyte act	0.0	9.4	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8 lymphocyte rest	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0

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Secondary CD8 lymphocyte act	0.0	0.0	KU-812 (Basophil) rest	0.0	0.0
CD4 lymphocyte none	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	0.0	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	0.0	0.0	Liver cirrhosis	**100.0**	**100.0**
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	0.0	0.0
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+ IL-18	0.0	0.0	NCI-H292 IL-4	0.0	0.0
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	0.0	0.0
NK Cells IL-2 rest	4.8	0.0	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	6.5	NCI-H292 IFN gamma	0.0	0.0
Two Way MLR 5 day	0.0	0.0	HPAEC none	0.0	0.0
Two Way MLR 7 day	0.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	0.0
PBMC rest	0.0	0.0	Lung fibroblast none	0.0	0.0
PBMC PWM	0.0	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	0.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes CD40L and IL-4	0.0	8.2	Dermal fibroblast CCD1070 rest	0.0	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast	9.5	0.0

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			CCD1070 TNF alpha		
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0
Dendritic cells none	0.0	0.0	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.0	0.0
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	19.3	38.7
Monocytes rest	0.0	0.0	IBD Crohn's	3.1	18.3
Monocytes LPS	0.0	0.0	Colon	11.9	7.4
Macrophages rest	0.0	0.0	Lung	0.0	0.0
Macrophages LPS	0.0	0.0	Thymus	4.8	0.0
HUVEC none	0.0	0.0	Kidney	0.0	0.0
HUVEC starved	0.0	0.0			

CNS_neurodegeneration_v1.0 Summary: Ag2484 Expression of this gene is low/undetectable (CT values >35) in all samples on this panel (data not shown).

Panel 1.3D Summary: Ag1783/Ag1781 Results from two experiments with the same probe/primer set are in good agreement, with significant expression of the GMAL163152_D gene limited to the spleen, an important site of secondary immune responses. Therefore, expression of this gene can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases. Ag2484/Ag1583 Expression of this gene is low/undetectable (CT values >35) in all samples on this panel (data not shown).

Panel 2.2 Summary: Ag1783/Ag1781/Ag1583 Expression of the GMAL163152_D gene in panel 2.2 is low/undetectable (CT values >35) in all samples (data not shown).

Panel 4D Summary: Ag1783/Ag1781 Two experiments using the same probe and primer set are in very good agreement, with significant expression of the GMAL163152_D gene limited to a sample from liver cirrhosis. Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used

for the diagnosis of liver cirrhosis. <u>Ag1583/Ag2484</u> Expression of this gene is low/undetectable (CT values >35) across all of the samples on this panel (data not shown).

AK. GMAC016856_A: GPCR

Expression of gene GMAC016856_A was assessed using the primer-probe set Ag1745, described in Table AKA. Results of the RTQ-PCR runs are shown in Tables AKB and AKC.

<u>Table AKA</u>. Probe Name Ag1745

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-acggagacccatgtatttcttc-3'	22	186	399
Probe	TET-5'-cacacttgtcctgccttgaaatctgg-3'-TAMRA	26	212	400
Reverse	5'-tcttgggcactgtaacagaagt-3'	22	241	401

<u>Table AKB</u>. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1745, Run 165940871	Tissue Name	Rel. Exp.(%) Ag1745, Run 165940871
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	5.1
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0

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Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	3.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	6.8	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	2.7	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	2.4
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0

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Colon ca. HCT-116	5.4	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	3.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table AKC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1745, Run 165806947	Tissue Name	Rel. Exp.(%) Ag1745, Run 165806947
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	1.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	3.8
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	2.9	Coronery artery SMC TNFalpha + IL-1beta	0.0

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CD8 lymphocyte act	0.0	Astrocytes rest	1.7
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	5.2
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	4.6
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	3.4
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	4.6
PBMC PHA-L	0.0	Lung fibroblast IL-4	3.6
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	4.6	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	6.8
Dendritic cells LPS	2.5	Dermal fibroblast IL-4	5.5
Dendritic cells anti-CD40	0.0	IBD Colitis 2	22.4

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Monocytes rest	0.0	IBD Crohn's	3.0
Monocytes LPS	4.1	Colon	0.0
Macrophages rest	0.0	Lung	8.7
Macrophages LPS	0.0	Thymus	4.9
HUVEC none	0.0	Kidney	0.0
HUVEC starved	2.4		

Panel 1.3D Summary: Ag1745 Significant expression of the GMAC016856_A gene is restricted to the spleen, an important site of secondary immune responses (CT = 33.5). Therefore, expression of this gene in spleen can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: Ag1745 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1745 Expression of the GMAC016856_A gene is limited to an IBD colitis sample (CT = 34.4). Interestingly, this gene does not appear to be expressed in the normal colon sample on this panel (CT = 40). Thus, expression of this gene may be used to distinguish IBD colitis from normal colon. Furthermore, therapeutic modulation of the acitvity of this gene or its protein product, using small molecule drugs or antibodies, may be of benefit in the treatment of inflammatory bowel disease.

AL. GMAC022882_F: GPCR

Expression of gene GMAC022882_F was assessed using the primer-probe set Ag1742, described in Table ALA. Results of the RTQ-PCR runs are shown in Tables ALB and ALC.

Table ALA. Probe Name Ag1742

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cttctacaccctggtgatacca-3'	22	840	402
Probe	TET-5'-tgctgaaccctctaatctacagcctca-3'-TAMRA	27	863	403

| Reverse | 5'-ttagtgcatccttcacgttctt-3' | | 22 | 895 | 404 |

Table ALB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1742, Run 165940868	Tissue Name	Rel. Exp.(%) Ag1742, Run 165940868
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	2.9	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	7.6
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	2.3
Spinal cord	2.5	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	4.6	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	**100.0**	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	5.2	Lung ca. (squam.) NCI-H596	0.0
Glioma SNB-19	0.0	Mammary gland	0.0
Glioma U251	3.1	Breast ca.* (pl.ef)	0.0

		MCF-7	
Glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	2.4	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	5.8	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	34.6	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	5.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	14.6
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	2.8	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table ALC. Panel 4D

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Tissue Name	Rel. Exp.(%) Ag1742, Run 165812570	Tissue Name	Rel. Exp.(%) Ag1742, Run 165812570
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	4.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	8.7
CD8 lymphocyte act	4.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	8.5	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0

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LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	4.1	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	9.4
Monocytes rest	8.1	IBD Crohn's	4.2
Monocytes LPS	0.0	Colon	4.9
Macrophages rest	0.0	Lung	1.4
Macrophages LPS	0.0	Thymus	4.8
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: <u>Ag1742</u> Highest expression of the GMAC022882_F gene is seen in an astrocytoma cell line (CT = 33). Therefore, expression of this gene may be used to distinguish astrocytoma cell lines from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of astrocytomas. In addition, low but significant expression is also seen in the spleen.

Panel 2.2 Summary: Ag1742 Expression of this gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1742 Significant expression of the GMAC022882_F gene is detected in a liver cirrhosis sample (CT = 33.1). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

AM. GMAC022882_E: GPCR

Expression of gene GMAC022882_E was assessed using the primer-probe set Ag1741, described in Table AMA. Results of the RTQ-PCR runs are shown in Tables AMB and AMC.

Table AMA. Probe Name Ag1741

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gctcttctccctctcaattgtt-3'	22	639	405
Probe	TET-5'-catgtttattctagtggccattctcaga-3'-TAMRA	28	672	406
Reverse	5'-tgtacctccctttccttgagtt-3'	22	703	407

Table AMB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1741, Run 165974806	Tissue Name	Rel. Exp.(%) Ag1741, Run 165974806
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	13.6	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	13.2
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0

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Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
Glioma SNB-19	0.0	Mammary gland	0.0
Glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
Glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca.	0.0

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		OVCAR-8	
Colorectal	5.9	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	25.5
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	8.4	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table AMC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1741, Run 165807997	Tissue Name	Rel. Exp.(%) Ag1741, Run 165807997
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0

Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN	0.0

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		gamma	
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	24.8
Monocytes rest	0.0	IBD Crohn's	10.8
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1741 The GMAC022882_E gene is expressed at detectable levels only in the spleen (CT=34.2), an important site of secondary immune responses. Therefore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: Ag1741 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1741 The GMAC022882_E transcript is expressed at detectable levels only in liver cirrhosis (CT=33.1). Furthermore, this transcript is not detected in normal liver in Panel 1.3D, suggesting that GMAC022882_E gene expression is unique to liver cirrhosis. The GMAC022882_E gene encodes a putative GPCR. Therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

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AN. GMAC022882_C: GPCR

Expression of gene GMAC022882_C was assessed using the primer-probe set Ag1740, described in Table ANA. Results of the RTQ-PCR runs are shown in Tables ANB and ANC.

Table ANA. Probe Name Ag1740

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cagcttcacactcccatgtatt-3'	22	172	408
Probe	TET-5'-tccttactcacttgtcatttattgacctca-3'-TAMRA	30	197	409
Reverse	5'-ttcgctaaggtttttaggtgtga-3'	22	242	410

Table ANB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1740, Run 165941041	Tissue Name	Rel. Exp.(%) Ag1740, Run 165941041
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	8.4
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0

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glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
Glioma SNB-19	0.0	Mammary gland	0.0
Glioma U251	6.0	Breast ca.* (pl.ef) MCF-7	0.0
Glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	7.5
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0

Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table ANC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1740, Run 165812562	Tissue Name	Rel. Exp.(%) Ag1740, Run 165812562
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0

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Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	· 0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	22.7
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0

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Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	4.7
HUVEC starved	0.0		

Panel 1.3D Summary: <u>Ag1740</u> Highest expression of the GMAC022882_C gene is detected in the spleen (CT = 34.1), an important site of secondary immune responses. Therefore, expression of this gene can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: <u>Ag1740</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag1740</u> Significant expression of the GMAC022882_C gene is detected in a liver cirrhosis sample (CT = 33.1). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

AO. GMAC022882_B: GPCR

Expression of gene GMAC022882_B was assessed using the primer-probe set Ag1739, described in Table AOA. Results of the RTQ-PCR runs are shown in Tables AOB and AOC.

Table AOA. Probe Name Ag1739

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gttgtgttggtcattgaggatt-3'	22	183	411
Probe	TET-5'-cctggctccacaaccccatgtattat-3'-TAMRA	26	205	412
Reverse	5'-agcaagcatccaagaatgataa-3'	22	243	413

Table AOB. Panel 1.3D

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Tissue Name	Rel. Exp.(%) Ag1739, Run 165974805	Tissue Name	Rel. Exp.(%) Ag1739, Run 165974805
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	8.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	5.2	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef)	0.0

		T47D	
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	4.1	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table AOC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1739, Run 165814423	Tissue Name	Rel. Exp.(%) Ag1739, Run 165814423
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0

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Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	3.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	2.2
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	1.8	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	100.0	Liver cirrhosis	46.7
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0

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Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	30.8
Monocytes rest	0.0	IBD Crohn's	3.2
Monocytes LPS	0.0	Colon	2.4
Macrophages rest	0.0	Lung	4.2
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1739 Highest expression of the GMAC022882_B gene is detected in the spleen (CT = 34.3), an important site of secondary immune responses. Therefore, expression of this gene in spleen can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: Ag1739 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

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Panel 4D Summary: Ag1739 Low but significant expression is also seen in a sample derived from a patient with IBD colitis (CT = 33.3), but not in normal colon. This observation suggests that the protein encoded by this gene may be involved in the inflammatory bowel disease process. Therefore, therapeutic modulation of the expression or function of this gene product, using small molecule drugs or antibodies, could potentially be of benefit in the treatment of inflammatory bowel disease.

AP. GMAC022207_C: GMAC022207_C_Cura_524_Homo_Sapiens_GPCR_like

Expression of gene GMAC022207_C was assessed using the primer-probe set Ag1738, described in Table APA. Results of the RTQ-PCR runs are shown in Table APB.

Table APA. Probe Name Ag1738

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggctgaacacaccaatgtattt-3'	22	179	414
Probe	TET-5'-ttcctaggcaatctctccttcattga-3'-TAMRA	26	202	415
Reverse	5'-catagccttgggttcaataaca-3'	22	243	416

Table APB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1738, Run 165812560	Tissue Name	Rel. Exp.(%) Ag1738, Run 165812560
Secondary Th1 act	2.7	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	3.1	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0

Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	3.1	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	3.7	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	5.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	1.9	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L	0.0	Dermal fibroblast	0.0

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and IL-4		CCD1070 rest	
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	35.8
Monocytes rest	0.0	IBD Crohn's	10.7
Monocytes LPS	0.0	Colon	4.7
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: <u>Ag1738</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: <u>Ag1738</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag1738</u> Significant expression of the GMAC022207_C gene is detected in a liver cirrhosis sample (CT = 34). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

AQ. GMAC022207_B: GPCR

Expression of gene GMAC022207_B was assessed using the primer-probe set Ag1737, described in Table AQA. Results of the RTQ-PCR runs are shown in Tables AQB and AQC.

<u>Table AQA</u>. Probe Name Ag1737

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Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-acaggcaaccattcagatgtaa-3'	22	25	417
Probe	TET-5'-agggtccgcccagagttctacattct-3'-TAMRA	26	70	418
Reverse	5'-tagatcagcaggaacaggaaga-3'	22	101	419

Table AQB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1737, Run 165974804	Tissue Name	Rel. Exp.(%) Ag1737, Run 165974804
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	2.6
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	6.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	5.3	Lung ca. (squam.) SW 900	0.0

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astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	**100.0**
glioma SNB-19	0.0	Mammary gland	0.0
Glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	5.8	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	86.5	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	10.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	1.3
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0

Kidney	0.0	Adipose	0.0

Table AQC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1737, Run 165814169	Tissue Name	Rel. Exp.(%) Ag1737, Run 165814169
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	3.4
Secondary Tr1 rest	13.6	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	10.3
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	4.8

LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	31.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	16.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	58.2
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	5.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	9.2
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	6.1
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	4.2
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	2.4
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1737 Expression of the GMAC022207_B gene is highest in a lung cancer cell line (CT = 33.5). In addition, significant expression is also detected in spleen (CT = 33.7). Therefore, expression of this gene can be used to distinguish lung cancer cell lines and spleen from the other samples on this panel. Furthermore, antibodies or small

5   molecule therapeutics that block the function of this GPCR may be useful as anti-

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inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases. In addition, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of lung cancer.

Panel 2.2 Summary: <u>Ag1737</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag1737</u> The GMAC022207_B gene is expressed at highest levels in liver cirrhosis. Normal liver does not express this transcript in panel 1.3 and 2.2 suggesting that expression of this gene may be induced by cirrhosis. Thus, the transcript or the protein encoded for by the transcript could be used diagnostically to identify liver cirrhosis.

Expression of the GMAC022207_B gene is also moderate in the lung mucoepidermoid cell line NCI-H292. In addition, expression of this gene is reduced in NCI-H292 cells treated with IL-13 and gamma interferon, both of which can effect the remodeling in the lung during asthma and emphysema. Therefore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs or antibodies, could be useful in treating tissue remodeling due to liver cirrhosis, asthma, or emphysema.

AR. GMAC011879_A: GPCR

Expression of gene GMAC011879_A was assessed using the primer-probe sets Ag2481 and Ag1735, described in Tables ARA and ARB. Results of the RTQ-PCR runs are shown in Tables ARC, ARD, ARE and ARF.

<u>Table ARA</u>. Probe Name Ag2481

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gggtaggactcagcacagtgta-3'	22	830	420
Probe	TET-5'-caacttgctcttccctgcgctgtag-3'-TAMRA	25	793	421
Reverse	5'-cgctgtcttctacgcctacata-3'	22	757	422

<u>Table ARB</u>. Probe Name Ag1735

Primers	Sequences	Length	Start Position	SEQ ID

				NO:
Forward	5'-agacgttggtaaccgagttcat-3'	22	15	423
Probe	TET-5'-agcacccagaataccgggtgttctta-3'-TAMRA	26	54	424
Reverse	5'-cccagagtagaggaagaggaaa-3'	22	88	425

Table ARC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2481, Run 208122024	Tissue Name	Rel. Exp.(%) Ag2481, Run 208122024
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	0.0
AD 2 Hippo	0.0	Control (Path) 4 Temporal Ctx	2.2
AD 3 Hippo	0.0	AD 1 Occipital Ctx	0.0
AD 4 Hippo	0.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	2.5	AD 3 Occipital Ctx	0.0
AD 6 Hippo	79.6	AD 4 Occipital Ctx	8.7
Control 2 Hippo	12.4	AD 5 Occipital Ctx	1.7
Control 4 Hippo	0.0	AD 6 Occipital Ctx	20.9
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	0.0	Control 2 Occipital Ctx	13.0
AD 2 Temporal Ctx	0.0	Control 3 Occipital Ctx	5.3
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	18.8	Control (Path) 1 Occipital Ctx	2.3
AD 5 Inf Temporal Ctx	31.2	Control (Path) 2 Occipital Ctx	0.0
AD 5 Sup Temporal Ctx	38.2	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	71.2	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	**100.0**	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	2.4
Control 2 Temporal Ctx	8.2	Control 3 Parietal Ctx	0.0
Control 3 Temporal	5.9	Control (Path) 1	0.0

Ctx		Parietal Ctx	
Control 3 Temporal Ctx	0.0	Control (Path) 2 Parietal Ctx	3.0
Control (Path) 1 Temporal Ctx	10.2	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	5.4	Control (Path) 4 Parietal Ctx	6.5

Table ARD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1735, Run 165533733	Rel. Exp.(%) Ag2481, Run 165534566	Tissue Name	Rel. Exp.(%) Ag1735, Run 165533733	Rel. Exp.(%) Ag2481, Run 165534566
Liver adenocarcinoma	0.0	0.0	Kidney (fetal)	0.0	0.0
Pancreas	10.4	6.0	Renal ca. 786-0	0.0	0.0
Pancreatic ca. CAPAN 2	0.0	0.0	Renal ca. A498	0.0	0.0
Adrenal gland	0.0	0.0	Renal ca. RXF 393	100.0	97.9
Thyroid	0.0	0.0	Renal ca. ACHN	0.0	0.0
Salivary gland	0.0	0.0	Renal ca. UO-31	0.0	0.0
Pituitary gland	0.0	0.0	Renal ca. TK-10	0.0	0.0
Brain (fetal)	0.0	9.0	Liver	0.0	0.0
Brain (whole)	16.4	0.0	Liver (fetal)	4.8	0.0
Brain (amygdala)	0.0	5.5	Liver ca. (hepatoblast) HepG2	0.0	0.0
Brain (cerebellum)	19.3	6.2	Lung	5.3	0.0
Brain (hippocampus)	0.0	0.0	Lung (fetal)	5.4	0.0
Brain (substantia nigra)	0.0	100.0	Lung ca. (small cell) LX-1	0.0	0.0
Brain (thalamus)	0.0	0.0	Lung ca. (small cell) NCI-H69	0.0	0.0
Cerebral Cortex	5.3	0.0	Lung ca. (s.cell var.) SHP-77	24.5	16.3

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Spinal cord	10.1	0.0	Lung ca. (large cell)NCI-H460	0.0	12.1
glio/astro U87-MG	0.0	0.0	Lung ca. (non-sm. cell) A549	0.0	0.0
glio/astro U-118-MG	0.0	0.0	Lung ca. (non-s.cell) NCI-H23	6.1	0.0
astrocytoma SW1783	8.7	0.0	Lung ca. (non-s.cell) HOP-62	0.0	1.9
neuro*; met SK-N-AS	0.0	0.0	Lung ca. (non-s.cl) NCI-H522	0.0	0.0
astrocytoma SF-539	0.0	0.0	Lung ca. (squam.) SW 900	0.0	6.8
astrocytoma SNB-75	0.0	9.8	Lung ca. (squam.) NCI-H596	0.0	0.0
glioma SNB-19	0.0	0.0	Mammary gland	0.0	0.0
glioma U251	0.0	0.0	Breast ca.* (pl.ef) MCF-7	0.0	0.0
glioma SF-295	0.0	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0	2.6
Heart (fetal)	0.0	0.0	Breast ca.* (pl.ef) T47D	0.0	0.0
Heart	0.0	0.0	Breast ca. BT-549	0.0	0.0
Skeletal muscle (fetal)	0.0	0.0	Breast ca. MDA-N	0.0	0.0
Skeletal muscle	5.2	19.9	Ovary	0.0	0.0
Bone marrow	0.0	0.0	Ovarian ca. OVCAR-3	0.0	0.0
Thymus	30.6	81.8	Ovarian ca. OVCAR-4	0.0	0.0
Spleen	19.8	14.6	Ovarian ca. OVCAR-5	0.0	0.0
Lymph node	30.1	53.2	Ovarian ca. OVCAR-8	0.0	0.0
Colorectal	4.9	0.0	Ovarian ca. IGROV-1	0.0	0.0
Stomach	0.0	0.0	Ovarian ca.*	4.3	0.0

			(ascites) SK-OV-3		
Small intestine	9.5	12.7	Uterus	0.0	0.0
Colon ca. SW480	0.0	0.0	Plancenta	0.0	0.0
Colon ca.* SW620(SW480 met)	0.0	4.7	Prostate	5.0	0.0
Colon ca. HT29	0.0	0.0	Prostate ca.* (bone met)PC-3	0.0	0.0
Colon ca. HCT-116	0.0	3.0	Testis	0.0	0.0
Colon ca. CaCo-2	0.0	0.0	Melanoma Hs688(A).T	0.0	0.0
Colon ca. tissue(ODO3866)	0.0	0.0	Melanoma* (met) Hs688(B).T	0.0	0.0
Colon ca. HCC-2998	0.0	0.0	Melanoma UACC-62	0.0	21.8
Gastric ca.* (liver met) NCI-N87	0.0	0.0	Melanoma M14	0.0	10.1
Bladder	0.0	0.0	Melanoma LOX IMVI	0.0	0.0
Trachea	15.9	0.0	Melanoma* (met) SK-MEL-5	0.0	0.0
Kidney	0.0	0.0	Adipose	0.0	0.0

Table ARE. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag1735, Run 173762017	Tissue Name	Rel. Exp.(%) Ag1735, Run 173762017
Normal Colon	9.8	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	20.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer	0.0	Kidney Cancer	0.0

(OD06297-04)		8120613	
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	0.0
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer 064010	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	22.7
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	11.6	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer (OD04566)	13.7
Ovarian Cancer 064008	**100.0**	Breast Cancer 1024	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	23.2	Breast Cancer Mets (OD04590-03)	11.6
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis (OD04655-05)	22.5
Ovarian Margin (OD06455-07)	0.0	Breast Cancer 064006	0.0
Normal Lung	20.6	Breast Cancer 9100266	9.1
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	9.5	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin	0.0	Breast cancer	10.2

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(OD03126)		(OD06083)	
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	9.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	13.3
Lung Margin (OD06081)	9.5	Liver Cancer 1025	50.7
Lung Cancer (OD04237-01)	22.5	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Melanoma Metastasis	0.0	Liver Cancer 6005-T	0.0
Ocular Melanoma Margin (Liver)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer 064003	0.0
Melanoma Margin (Lung)	10.5	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer 1023	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	11.4	Bladder Cancer A302173	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	5.3
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	12.6
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	12.4
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table ARF. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1735, Run 165355439	Rel. Exp.(%) Ag2481, Run 164317770	Tissue Name	Rel. Exp.(%) Ag1735, Run 165355439	Rel. Exp.(%) Ag2481, Run 164317770
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN	0.0	0.0

			gamma		
Secondary Tr1 act	0.0	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	1.2	1.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.6
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0
Primary Th1 rest	8.3	3.7	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0
Primary Th2 rest	3.5	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	0.0	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0	0.0
CD45RA CD4 lymphocyte act	0.0	0.0	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.8	0.0	Astrocytes rest	0.5	0.0
Secondary CD8 lymphocyte rest	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0
Secondary CD8 lymphocyte act	0.0	0.0	KU-812 (Basophil) rest	0.0	0.0
CD4 lymphocyte none	1.0	0.0	KU-812 (Basophil) PMA/ionomycin	0.0	0.0

2ry Th1/Th2/Tr1_anti-CD95 CH11	1.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	4.7	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	1.1	0.0	Liver cirrhosis	2.8	6.5
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	0.0	0.0
LAK cells IL-2+IFN gamma	3.4	0.0	NCI-H292 none	5.0	5.0
LAK cells IL-2+IL-18	1.3	0.0	NCI-H292 IL-4	5.9	0.6
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	3.4	1.5
NK Cells IL-2 rest	0.0	0.0	NCI-H292 IL-13	5.0	0.3
Two Way MLR 3 day	0.0	1.6	NCI-H292 IFN gamma	3.7	0.2
Two Way MLR 5 day	0.0	0.3	HPAEC none	0.0	0.0
Two Way MLR 7 day	0.0	0.8	HPAEC TNF alpha + IL-1 beta	0.0	0.0
PBMC rest	0.0	0.0	Lung fibroblast none	0.0	0.3
PBMC PWM	2.3	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	0.0
Ramos (B cell) none	35.1	27.4	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	**100.0**	**100.0**	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	2.0	2.3	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes CD40L and IL-4	11.5	9.0	Dermal fibroblast CCD1070 rest	0.0	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0

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Dendritic cells none	1.1	0.0	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.0	0.0
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	0.0	0.0
Monocytes rest	0.9	0.0	IBD Crohn's	0.0	0.3
Monocytes LPS	0.0	0.0	Colon	1.1	1.4
Macrophages rest	1.2	0.2	Lung	0.0	1.3
Macrophages LPS	1.2	0.0	Thymus	0.0	0.0
HUVEC none	0.0	0.0	Kidney	20.4	26.2
HUVEC starved	0.0	0.0			

CNS_neurodegeneration_v1.0 Summary: <u>Ag2481</u> Expression of the GMAC011879_A gene is upregulated in the temporal cortex of Alzheimer's disease patients. Therefore, blockade of this receptor may be of use in the treatment of this disease and decrease neuronal death. Please see Panel 1.3D for further discussion of potential utility of this gene in the treatment of CNS disorders.

Panel 1.3D Summary: <u>Ag1735/2481</u> Expression of the GMAC011879_A gene was assessed in two independent runs, each run with a different probe and primer set. There was good concordance between the two runs with the consistent highest expression seen in a sample derived from a renal cell cancer cell line (RXF 393). In addition, there was relatively high expression in a sample derived from substantia nigra, but only in one of the runs (run Id#165534566). This run also showed substantial expression associated with thymus and lymph node tissue. Thus, the expression of this gene could be used to distinguish the above listed samples from other samples in the panel. In addition, therapeutic modulation of the activity of this gene or its product product, using small molecule drugs, antibodies or protein therapeutics, may be of use in the treatment of kidney cancer.

This gene represents a novel G-protein coupled receptor (GPCR) with low, but significant expression in the brain. The GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act

at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and α2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the α-adrenergic receptors have been implicated in memory. Therefore this gene may be of use as a small molecule target for the treatment of any of the described diseases.

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2

receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response. The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic

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receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating

5   disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA

10   receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats.
15   Neuroreport 1998 Dec 1;9(17):3955-9 Related Articles, Books, LinkOut

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01

20   mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, p < 0.05). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, p < 0.05). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a

25   potentially useful biological target for the reduction of brain injury.

Panel 2.2 Summary: Ag1735 Significant expression of the GMAC011879_A gene is seen exclusively in an ovarian cancer sample (CT = 33.9). Therefore, expression of this gene may be used to distinguish ovarian cancers from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene, using small

30   molecule drugs or antibodies, may be beneficial in the treatment of ovarian cancer.

Panel 4D Summary: <u>Ag1735/Ag2481</u> Results from two experiments using different probe/primer sets are in good agreement. Expression of the GMAC011879_A gene is seen in Ramos B cells, B cells treated with CD40L and IL-4, and kidney. This transcript appears to be expressed primarily in actively proliferating B cells and a B cell lymphoma. In normal B cells, the stimulus is one that induces not only proliferation but also survival and differentiation; proliferation alone is not sufficient for expression of this gene based on the lack of expression in B cells stimulated by poke weed mitogen. Therefore, the transcript or the protein encoded for by the transcript could be used to identify B cells undergoing proliferation/differentiation. Furthermore, therapeutics designed with the protein encoded for by this transcript could be helpful in the treatment of diseases that include the inappropriate proliferation of differentiation of B cells including lupus, allergy, and atopic asthma.

AS. GMAC011571_A/CG149443-01: Olfactory Receptor

Expression of gene GMAC011571_A (also known as CG149443-01) was assessed using the primer-probe sets Ag1734 and Ag1723, described in Tables ASA and ASB. Results of the RTQ-PCR runs are shown in Tables ASC and ASD.

Table ASA. Probe Name Ag1734

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gggaagttccttacccttttct-3'	22	826	426
Probe	TET-5'-ccccatgttaaaccctgtcatctataca-3'-TAMRA	28	861	427
Reverse	5'-tcagtgcaccttttacatcctt-3'	22	898	428

Table ASB. Probe Name Ag1723

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-agcatgtcctctttgtgtttgt-3'	22	86	429
Probe	TET-5'-ccttgtgaccttagtgggcaacatca-3'-TAMRA	26	120	430
Reverse	5'-ccaggtgggagatcaagataat-3'	22	148	431

Table ASC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1734, Run	Tissue Name	Rel. Exp.(%) Ag1734, Run

	165940872		165940872
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	5.6	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	9.3
Brain (amygdala)	6.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	5.7
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	11.2
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	11.1
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0

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Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	5.7	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	13.9
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table ASD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1723, Run 165767112	Rel. Exp.(%) Ag1734, Run 165813047	Tissue Name	Rel. Exp.(%) Ag1723, Run 165767112	Rel. Exp.(%) Ag1734, Run 165813047
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	4.7	0.0	HUVEC IFN	0.0	0.0

			gamma		
Secondary Tr1 act	2.1	10.8	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	3.4	0.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	4.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	4.5	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	10.1	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0
Primary Th1 rest	9.4	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	9.9	0.0	Small airway epithelium TNFalpha + IL-1beta	15.2	25.2
CD45RA CD4 lymphocyte act	0.0	0.0	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	3.6	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	4.7	16.5
Secondary CD8 lymphocyte rest	14.4	9.5	Astrocytes TNFalpha + IL-1beta	0.0	25.5
Secondary CD8 lymphocyte act	4.5	0.0	KU-812 (Basophil) rest	10.4	9.9
CD4 lymphocyte none	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	22.7	5.1

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2ry Th1/Th2/Tr1_anti-CD95 CH11	21.6	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	0.0	12.9	Liver cirrhosis	**100.0**	**100.0**
LAK cells IL-2+IL-12	4.9	11.7	Lupus kidney	0.0	35.4
LAK cells IL-2+IFN gamma	0.0	12.2	NCI-H292 none	0.0	0.0
LAK cells IL-2+IL-18	5.4	28.9	NCI-H292 IL-4	0.0	37.4
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	2.7	8.5
NK Cells IL-2 rest	0.0	15.2	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	0.0	NCI-H292 IFN gamma	3.9	0.0
Two Way MLR 5 day	0.0	0.0	HPAEC none	0.0	0.0
Two Way MLR 7 day	4.8	0.0	HPAEC TNF alpha + IL-1 beta	0.0	0.0
PBMC rest	0.0	0.0	Lung fibroblast none	4.5	0.0
PBMC PWM	11.3	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	0.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes CD40L and IL-4	13.1	11.3	Dermal fibroblast CCD1070 rest	5.2	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	23.5
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0

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Dendritic cells none	0.0	0.0	Dermal fibroblast IFN gamma	0.0	5.8
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.0	0.0
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	28.7	34.6
Monocytes rest	0.0	0.0	IBD Crohn's	4.9	0.0
Monocytes LPS	0.0	0.0	Colon	23.0	13.8
Macrophages rest	8.8	0.0	Lung	0.0	0.0
Macrophages LPS	0.0	9.2	Thymus	14.0	50.0
HUVEC none	0.0	0.0	Kidney	39.8	19.3
HUVEC starved	0.0	11.6			

Panel 1.3D Summary: <u>Ag1734</u> Significant expression of the GMAC011571_A gene is restricted to the spleen, an important site of secondary immune responses (CT = 34.2). Therefore, expression of this gene can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: <u>Ag1734</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag1723/Ag1734</u> Results from two experiments using different probe/primer sets show reasonable agreement. Significant expression of this gene is primarily detected in a liver cirrhosis sample (CT = 33-34). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

AT. GMAC008745_A and GMAC016626_A: GPCR

Expression of gene GMAC008745_A and variant GMAC016626_A was assessed using the primer-probe sets Ag1566, Ag1570 and Ag1733, described in Tables ATA, ATB

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and ATC. Results of the RTQ-PCR runs are shown in Tables ATD, ATE, ATF, ATG and ATH.

Table ATA. Probe Name Ag1566

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cagctcctcctcctagtgtttt-3'	22	83	432
Probe	TET-5'-cctctgtgctctatgtggcaagcatt-3'-TAMRA	26	105	433
Reverse	5'-tggtcacagaaaacacaatgag-3'	22	143	434

Table ATB. Probe Name Ag1570

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tttgatgcagttctcactcctt-3'	22	833	435
Probe	TET-5'-tctgaatccagttgtctatacattcagga-3'-TAMRA	29	856	436
Reverse	5'-tattgctgccttcatctcctta-3'	22	886	437

5   Table ATC. Probe Name Ag1733

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tttgatgcagttctcactcctt-3'	22	833	438
Probe	TET-5'-tctgaatccagttgtctatacattcagga-3'-TAMRA	29	856	439
Reverse	5'-tattgctgccttcatctcctta-3'	22	886	440

Table ATD. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag1566, Run 228020431	Tissue Name	Rel. Exp.(%) Ag1566, Run 228020431
AD 1 Hippo	9.1	Control (Path) 3 Temporal Ctx	10.7
AD 2 Hippo	36.1	Control (Path) 4 Temporal Ctx	74.2
AD 3 Hippo	14.1	AD 1 Occipital Ctx	19.2
AD 4 Hippo	29.9	AD 2 Occipital Ctx (Missing)	1.1
AD 5 Hippo	**100.0**	AD 3 Occipital Ctx	21.2
AD 6 Hippo	80.1	AD 4 Occipital Ctx	62.4

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Control 2 Hippo	21.0	AD 5 Occipital Ctx	24.8
Control 4 Hippo	28.5	AD 6 Occipital Ctx	25.2
Control (Path) 3 Hippo	20.0	Control 1 Occipital Ctx	4.7
AD 1 Temporal Ctx	16.7	Control 2 Occipital Ctx	35.6
AD 2 Temporal Ctx	39.5	Control 3 Occipital Ctx	24.1
AD 3 Temporal Ctx	18.2	Control 4 Occipital Ctx	17.2
AD 4 Temporal Ctx	70.7	Control (Path) 1 Occipital Ctx	96.6
AD 5 Inf Temporal Ctx	93.3	Control (Path) 2 Occipital Ctx	11.2
AD 5 Sup Temporal Ctx	43.8	Control (Path) 3 Occipital Ctx	11.7
AD 6 Inf Temporal Ctx	77.9	Control (Path) 4 Occipital Ctx	34.9
AD 6 Sup Temporal Ctx	92.7	Control 1 Parietal Ctx	18.0
Control 1 Temporal Ctx	21.2	Control 2 Parietal Ctx	67.8
Control 2 Temporal Ctx	21.3	Control 3 Parietal Ctx	18.4
Control 3 Temporal Ctx	16.8	Control (Path) 1 Parietal Ctx	66.0
Control 3 Temporal Ctx	25.3	Control (Path) 2 Parietal Ctx	24.0
Control (Path) 1 Temporal Ctx	72.7	Control (Path) 3 Parietal Ctx	12.7
Control (Path) 2 Temporal Ctx	21.2	Control (Path) 4 Parietal Ctx	69.3

Table ATE. General_screening_panel_v1.5

Tissue Name	Rel. Exp.(%) Ag1566, Run 228632352	Tissue Name	Rel. Exp.(%) Ag1566, Run 228632352
Adipose	5.1	Renal ca. TK-10	24.8
Melanoma* Hs688(A).T	6.4	Bladder	24.8
Melanoma* Hs688(B).T	12.5	Gastric ca. (liver met.) NCI-N87	20.2
Melanoma* M14	6.1	Gastric ca. KATO III	14.7
Melanoma*	9.0	Colon ca. SW-948	2.3

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LOXIMVI			
Melanoma* SK-MEL-5	8.2	Colon ca. SW480	5.1
Squamous cell carcinoma SCC-4	1.0	Colon ca.* (SW480 met) SW620	1.3
Testis Pool	36.3	Colon ca. HT29	3.0
Prostate ca.* (bone met) PC-3	1.9	Colon ca. HCT-116	25.3
Prostate Pool	10.7	Colon ca. CaCo-2	7.5
Placenta	12.6	Colon cancer tissue	9.7
Uterus Pool	11.7	Colon ca. SW1116	3.9
Ovarian ca. OVCAR-3	11.6	Colon ca. Colo-205	0.8
Ovarian ca. SK-OV-3	69.3	Colon ca. SW-48	0.7
Ovarian ca. OVCAR-4	1.3	Colon Pool	25.2
Ovarian ca. OVCAR-5	18.4	Small Intestine Pool	17.0
Ovarian ca. IGROV-1	6.4	Stomach Pool	12.4
Ovarian ca. OVCAR-8	11.8	Bone Marrow Pool	10.8
Ovary	6.0	Fetal Heart	5.1
Breast ca. MCF-7	5.0	Heart Pool	7.4
Breast ca. MDA-MB-231	14.9	Lymph Node Pool	12.3
Breast ca. BT 549	2.5	Fetal Skeletal Muscle	11.2
Breast ca. T47D	0.5	Skeletal Muscle Pool	22.5
Breast ca. MDA-N	8.2	Spleen Pool	9.0
Breast Pool	23.0	Thymus Pool	11.4
Trachea	7.8	CNS cancer (glio/astro) U87-MG	23.2
Lung	11.5	CNS cancer (glio/astro) U-118-MG	37.4
Fetal Lung	33.7	CNS cancer (neuro;met) SK-N-AS	12.2
Lung ca. NCI-N417	0.6	CNS cancer (astro) SF-539	6.0
Lung ca. LX-1	15.3	CNS cancer (astro) SNB-75	17.7
Lung ca. NCI-H146	1.8	CNS cancer (glio) SNB-19	8.7

Lung ca. SHP-77	10.3	CNS cancer (glio) SF-295	45.7
Lung ca. A549	0.4	Brain (Amygdala) Pool	6.8
Lung ca. NCI-H526	1.5	Brain (cerebellum)	17.6
Lung ca. NCI-H23	20.7	Brain (fetal)	12.2
Lung ca. NCI-H460	55.5	Brain (Hippocampus) Pool	10.7
Lung ca. HOP-62	5.0	Cerebral Cortex Pool	13.0
Lung ca. NCI-H522	6.6	Brain (Substantia nigra) Pool	10.2
Liver	0.7	Brain (Thalamus) Pool	15.9
Fetal Liver	10.2	Brain (whole)	11.8
Liver ca. HepG2	7.5	Spinal Cord Pool	9.5
Kidney Pool	23.3	Adrenal Gland	8.7
Fetal Kidney	34.9	Pituitary gland Pool	2.7
Renal ca. 786-0	16.2	Salivary Gland	4.6
Renal ca. A498	18.8	Thyroid (female)	0.4
Renal ca. ACHN	**100.0**	Pancreatic ca. CAPAN2	8.5
Renal ca. UO-31	13.5	Pancreas Pool	23.7

Table ATF. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1570, Run 165534728	Rel. Exp.(%) Ag1733, Run 165933478	Tissue Name	Rel. Exp.(%) Ag1570, Run 165534728	Rel. Exp.(%) Ag1733, Run 165933478
Liver adenocarcinoma	4.9	3.5	Kidney (fetal)	4.6	5.9
Pancreas	11.7	1.6	Renal ca. 786-0	22.2	10.9
Pancreatic ca. CAPAN 2	2.8	4.6	Renal ca. A498	26.2	2.7
Adrenal gland	0.0	3.9	Renal ca. RXF 393	9.6	13.6
Thyroid	4.9	0.0	Renal ca. ACHN	57.0	36.3
Salivary gland	6.7	2.6	Renal ca. UO-31	10.1	5.0
Pituitary gland	1.8	1.0	Renal ca. TK-10	15.7	3.7
Brain (fetal)	5.1	1.2	Liver	1.8	2.0
Brain (whole)	32.3	1.5	Liver (fetal)	10.0	3.6
Brain (amygdala)	12.2	0.0	Liver ca.	21.6	4.7

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			(hepatoblast) HepG2		
Brain (cerebellum)	8.7	9.3	Lung	0.0	0.0
Brain (hippocampus)	0.0	0.0	Lung (fetal)	4.2	3.9
Brain (substantia nigra)	0.0	8.6	Lung ca. (small cell) LX-1	14.2	6.8
Brain (thalamus)	2.4	0.0	Lung ca. (small cell) NCI-H69	12.0	3.9
Cerebral Cortex	1.7	2.5	Lung ca. (s.cell var.) SHP-77	6.9	2.9
Spinal cord	6.7	0.0	Lung ca. (large cell)NCI-H460	27.2	1.8
glio/astro U87-MG	11.0	5.0	Lung ca. (non-sm. cell) A549	3.0	0.0
glio/astro U-118-MG	55.5	4.9	Lung ca. (non-s.cell) NCI-H23	16.3	5.8
astrocytoma SW1783	37.1	22.2	Lung ca. (non-s.cell) HOP-62	2.3	0.0
neuro*; met SK-N-AS	3.3	2.4	Lung ca. (non-s.cl) NCI-H522	0.0	0.0
astrocytoma SF-539	12.7	7.0	Lung ca. (squam.) SW 900	5.5	0.0
astrocytoma SNB-75	9.6	0.6	Lung ca. (squam.) NCI-H596	13.6	3.5
glioma SNB-19	37.4	14.2	Mammary gland	0.0	0.0
glioma U251	**100.0**	2.9	Breast ca.* (pl.ef) MCF-7	11.8	4.5
glioma SF-295	30.8	2.2	Breast ca.* (pl.ef) MDA-MB-231	5.3	1.3
Heart (fetal)	0.0	0.0	Breast ca.* (pl.ef) T47D	0.0	0.0
Heart	7.7	0.0	Breast ca. BT-549	5.1	0.0

Skeletal muscle (fetal)	2.5	4.2	Breast ca. MDA-N	10.9	0.5
Skeletal muscle	0.0	2.9	Ovary	0.0	0.0
Bone marrow	2.4	1.9	Ovarian ca. OVCAR-3	11.6	5.1
Thymus	0.0	1.3	Ovarian ca. OVCAR-4	2.4	0.0
Spleen	0.0	**100.0**	Ovarian ca. OVCAR-5	11.5	2.2
Lymph node	9.1	0.0	Ovarian ca. OVCAR-8	13.2	4.6
Colorectal	6.3	9.5	Ovarian ca. IGROV-1	0.0	2.4
Stomach	5.8	3.0	Ovarian ca.* (ascites) SK-OV-3	25.0	47.6
Small intestine	9.9	0.0	Uterus	2.1	0.0
Colon ca. SW480	0.0	0.0	Plancenta	0.0	2.4
Colon ca.* SW620(SW480 met)	0.0	0.0	Prostate	2.2	0.0
Colon ca. HT29	0.0	1.5	Prostate ca.* (bone met)PC-3	2.2	0.0
Colon ca. HCT-116	12.2	3.4	Testis	23.7	10.4
Colon ca. CaCo-2	0.0	1.1	Melanoma Hs688(A).T	2.1	0.0
Colon ca. tissue(ODO3866)	7.7	1.4	Melanoma* (met) Hs688(B).T	2.5	1.0
Colon ca. HCC-2998	20.3	3.3	Melanoma UACC-62	8.7	2.4
Gastric ca.* (liver met) NCI-N87	8.2	0.7	Melanoma M14	21.2	15.0
Bladder	15.8	8.8	Melanoma LOX IMVI	3.5	0.0
Trachea	0.0	0.0	Melanoma* (met) SK-MEL-5	0.0	0.0
Kidney	0.0	3.0	Adipose	8.7	1.3

Table ATG. Panel 2.2

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Tissue Name	Rel. Exp.(%) Ag1570, Run 173968823	Rel. Exp.(%) Ag1733, Run 174111806	Tissue Name	Rel. Exp.(%) Ag1570, Run 173968823	Rel. Exp.(%) Ag1733, Run 174111806
Normal Colon	8.2	4.2	Kidney Margin (OD04348)	80.7	88.9
Colon cancer (OD06064)	2.7	3.1	Kidney malignant cancer (OD06204B)	40.1	38.4
Colon Margin (OD06064)	0.0	0.0	Kidney normal adjacent tissue (OD06204E)	0.0	2.8
Colon cancer (OD06159)	0.0	0.0	Kidney Cancer (OD04450-01)	**100.0**	74.2
Colon Margin (OD06159)	10.3	0.0	Kidney Margin (OD04450-03)	10.4	15.6
Colon cancer (OD06297-04)	0.0	9.0	Kidney Cancer 8120613	0.0	0.0
Colon Margin (OD06297-015)	12.2	4.3	Kidney Margin 8120614	8.4	0.0
CC Gr.2 ascend colon (ODO3921)	2.9	8.0	Kidney Cancer 9010320	6.8	4.3
CC Margin (ODO3921)	3.7	14.3	Kidney Margin 9010321	2.1	7.9
Colon cancer metastasis (OD06104)	0.0	0.0	Kidney Cancer 8120607	4.8	0.0
Lung Margin (OD06104)	2.6	0.0	Kidney Margin 8120608	0.0	0.0
Colon mets to lung (OD04451-01)	34.4	24.5	Normal Uterus	7.6	1.6
Lung Margin (OD04451-02)	22.2	22.5	Uterine Cancer 064011	0.0	4.0
Normal Prostate	0.0	9.5	Normal Thyroid	0.0	0.0
Prostate Cancer (OD04410)	14.9	7.5	Thyroid Cancer 064010	11.2	12.9
Prostate Margin (OD04410)	9.9	6.0	Thyroid Cancer A302152	16.4	40.3
Normal Ovary	0.0	0.0	Thyroid Margin A302153	0.0	0.0
Ovarian cancer (OD06283-03)	0.0	5.6	Normal Breast	57.8	23.3
Ovarian Margin	6.2	19.2	Breast Cancer	21.8	16.4

(OD06283-07)			(OD04566)		
Ovarian Cancer 064008	10.2	35.4	Breast Cancer 1024	6.1	18.2
Ovarian cancer (OD06145)	0.0	0.0	Breast Cancer (OD04590-01)	6.3	0.0
Ovarian Margin (OD06145)	7.9	17.9	Breast Cancer Mets (OD04590-03)	7.0	28.7
Ovarian cancer (OD06455-03)	24.7	24.5	Breast Cancer Metastasis (OD04655-05)	24.1	48.0
Ovarian Margin (OD06455-07)	2.4	4.1	Breast Cancer 064006	11.6	0.0
Normal Lung	8.7	18.6	Breast Cancer 9100266	15.8	4.8
Invasive poor diff. lung adeno (ODO4945-01	10.3	0.0	Breast Margin 9100265	0.0	0.0
Lung Margin (ODO4945-03)	28.3	14.8	Breast Cancer A209073	3.6	0.0
Lung Malignant Cancer (OD03126)	2.5	0.0	Breast Margin A2090734	14.1	17.6
Lung Margin (OD03126)	3.6	0.0	Breast cancer (OD06083)	11.6	30.8
Lung Cancer (OD05014A)	11.6	8.6	Breast cancer node metastasis (OD06083)	7.8	18.0
Lung Margin (OD05014B)	23.8	8.8	Normal Liver	46.0	94.6
Lung cancer (OD06081)	0.0	11.3	Liver Cancer 1026	0.0	0.0
Lung Margin (OD06081)	4.1	9.3	Liver Cancer 1025	18.0	14.5
Lung Cancer (OD04237-01)	0.0	0.0	Liver Cancer 6004-T	9.7	0.0
Lung Margin (OD04237-02)	30.6	32.5	Liver Tissue 6004-N	0.0	9.6
Ocular Melanoma Metastasis	3.5	0.0	Liver Cancer 6005-T	0.0	0.0
Ocular Melanoma Margin (Liver)	3.2	7.7	Liver Tissue 6005-N	0.0	0.0
Melanoma	4.3	6.0	Liver Cancer	21.0	36.1

Metastasis			064003		
Melanoma Margin (Lung)	1.8	0.0	Normal Bladder	3.6	19.3
Normal Kidney	9.4	18.7	Bladder Cancer 1023	10.3	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	40.3	33.2	Bladder Cancer A302173	13.5	26.8
Kidney Margin (OD04338)	34.4	15.1	Normal Stomach	16.7	30.4
Kidney Ca Nuclear grade ½ (OD04339)	46.0	**100.0**	Gastric Cancer 9060397	0.0	0.0
Kidney Margin (OD04339)	0.0	9.4	Stomach Margin 9060396	0.0	8.4
Kidney Ca, Clear cell type (OD04340)	25.5	15.1	Gastric Cancer 9060395	11.8	7.6
Kidney Margin (OD04340)	14.3	29.7	Stomach Margin 9060394	11.0	7.4
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	0.0	Gastric Cancer 064005	3.4	18.8

Table ATH. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1566, Run 163479216	Rel. Exp.(%) Ag1570, Run 163480432	Rel. Exp.(%) Ag1733, Run 165813007	Tissue Name	Rel. Exp.(%) Ag1566, Run 163479216	Rel. Exp.(%) Ag1570, Run 163480432	Rel. Exp.(%) Ag1733, Run 165813007
Secondary Th1 act	22.5	29.1	12.7	HUVEC IL-1beta	10.6	9.7	5.8
Secondary Th2 act	5.6	6.1	2.1	HUVEC IFN gamma	27.0	14.6	7.2
Secondary Tr1 act	10.4	6.0	2.9	HUVEC TNF alpha + IFN gamma	17.7	12.4	4.3
Secondary Th1 rest	0.0	14.3	7.6	HUVEC TNF alpha + IL4	19.8	11.9	10.2
Secondary Th2 rest	7.0	13.7	1.4	HUVEC IL-11	25.9	6.9	2.7
Secondary Tr1	7.9	9.7	2.3	Lung	34.4	35.4	13.4

rest				Microvascular EC none			
Primary Th1 act	33.4	39.8	7.3	Lung Microvascular EC TNFalpha + IL-1beta	31.2	23.2	13.7
Primary Th2 act	33.7	50.3	21.8	Microvascular Dermal EC none	37.9	71.2	11.7
Primary Tr1 act	47.6	55.9	24.5	Microsvasular Dermal EC TNFalpha + IL-1beta	38.2	18.4	7.7
Primary Th1 rest	39.0	34.9	18.8	Bronchial epithelium TNFalpha + IL1beta	59.9	28.1	3.6
Primary Th2 rest	20.2	10.1	5.5	Small airway epithelium none	6.0	3.7	1.5
Primary Tr1 rest	15.3	16.3	5.1	Small airway epithelium TNFalpha + IL-1beta	49.3	25.7	12.3
CD45RA CD4 lymphocyte act	19.2	9.5	14.3	Coronery artery SMC rest	11.8	4.7	4.0
CD45RO CD4 lymphocyte act	25.7	16.7	13.4	Coronery artery SMC TNFalpha + IL-1beta	5.2	4.5	0.8
CD8 lymphocyte act	28.9	27.2	21.6	Astrocytes rest	72.2	38.2	44.1
Secondary CD8 lymphocyte rest	25.9	28.9	14.6	Astrocytes TNFalpha + IL-1beta	29.3	50.0	61.6
Secondary CD8 lymphocyte act	6.3	13.5	15.2	KU-812 (Basophil) rest	71.7	24.5	23.8
CD4 lymphocyte none	10.4	2.5	12.9	KU-812 (Basophil) PMA/ionomycin	**100.0**	**100.0**	48.3
2ry Th1/Th2/Tr1_anti-CD95 CH11	9.5	12.2	6.7	CCD1106 (Keratinocytes) none	20.9	28.9	5.9
LAK cells rest	14.9	21.5	5.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.7	9.0	29.3
LAK cells IL-2	30.8	27.7	17.3	Liver cirrhosis	50.3	92.7	**100.0**

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LAK cells IL-2+IL-12	18.8	9.9	17.7	Lupus kidney	20.9	6.0	15.2
LAK cells IL-2+IFN gamma	43.2	27.0	38.2	NCI-H292 none	25.0	16.3	12.5
LAK cells IL-2+IL-18	27.5	27.5	25.0	NCI-H292 IL-4	23.5	23.5	13.4
LAK cells PMA/ionomycin	20.3	21.6	11.5	NCI-H292 IL-9	19.1	25.0	10.3
NK Cells IL-2 rest	17.0	27.4	7.2	NCI-H292 IL-13	10.7	12.4	3.3
Two Way MLR 3 day	22.2	31.0	18.3	NCI-H292 IFN gamma	24.5	14.4	6.3
Two Way MLR 5 day	17.2	9.0	7.1	HPAEC none	23.7	9.1	7.2
Two Way MLR 7 day	19.1	19.3	9.3	HPAEC TNF alpha + IL-1 beta	38.7	12.9	11.7
PBMC rest	2.3	0.0	5.3	Lung fibroblast none	22.5	42.9	18.2
PBMC PWM	81.8	51.4	14.2	Lung fibroblast TNF alpha + IL-1 beta	15.6	17.9	18.6
PBMC PHA-L	23.8	22.4	6.4	Lung fibroblast IL-4	76.3	46.3	20.0
Ramos (B cell) none	12.7	6.7	7.6	Lung fibroblast IL-9	42.0	23.0	17.0
Ramos (B cell) ionomycin	37.9	12.0	6.7	Lung fibroblast IL-13	44.8	40.1	16.6
B lymphocytes PWM	58.2	35.4	7.9	Lung fibroblast IFN gamma	54.7	42.3	13.2
B lymphocytes CD40L and IL-4	37.6	20.6	9.6	Dermal fibroblast CCD1070 rest	23.8	48.0	27.7
EOL-1 dbcAMP	30.6	27.5	12.8	Dermal fibroblast CCD1070 TNF alpha	43.2	34.6	24.1
EOL-1 dbcAMP PMA/ionomycin	36.1	24.3	15.2	Dermal fibroblast CCD1070 IL-1 beta	37.9	23.7	12.6
Dendritic cells none	25.2	32.3	7.9	Dermal fibroblast IFN gamma	17.3	16.7	5.9
Dendritic cells	9.5	11.2	2.7	Dermal	47.0	59.9	12.9

LPS				fibroblast IL-4			
Dendritic cells anti-CD40	28.5	9.6	8.7	IBD Colitis 2	12.9	6.9	4.0
Monocytes rest	9.4	9.3	3.5	IBD Crohn's	7.5	0.0	0.5
Monocytes LPS	19.1	23.2	14.6	Colon	15.1	28.3	28.3
Macrophages rest	21.3	17.3	13.3	Lung	11.2	7.1	4.0
Macrophages LPS	8.8	5.8	1.9	Thymus	66.9	78.5	23.8
HUVEC none	20.4	10.4	21.5	Kidney	68.3	86.5	21.3
HUVEC starved	31.6	15.7	24.7				

CNS_neurodegeneration_v1.0 Summary: <u>Ag1566</u> No difference was detected in the expression of the GMAC008745_A gene in the postmortem brains of Alzheimer's diseased patients when compared to controls; however this panel demonstrates the expression of this gene in the brains of an independent group of subjects. See General_screening_panel_v1.5 for a discussion of utility in the central nervous system.

General_screening_panel_v1.5 Summary: <u>Ag1566</u> This gene is expressed at low to moderate levels in the majority of samples on this panel. Expression of the GMAC008745_A gene is highest in a sample derived from renal cell cancer cell line ACHN (CT = 28). In addition, there is similarly high expression in samples derived from a lung cancer cell line and an ovarian cancer cell line. Thus, therapeutic modulation of this gene, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of renal cell cancer, lung cancer or ovarian cancer.

Among tissues with metabolic activity, the GMAC008745_A gene is expressed at moderate levels in pancreas, adrenal gland, heart, skeletal muscle and fetal liver and at low levels in pituitary gland and adipose. Interestingly, expression of this gene is significantly higher in fetal liver (CT = 31.3) than in adult liver (CT = 35.3). This observation suggests that expression of this gene can be used to distinguish fetal from adult liver; it also suggests that this protein product may enhance liver growth or development in the fetus and thus may also act in a regenerative capacity in the adult. Furthermore, expression of this gene in metabolic tissues suggests that this gene may play a role in cardiovascular disease or metabolic diseases, such as obesity and diabetes.

This gene represents a novel G-protein coupled receptor (GPCR) that also shows moderate expression in the brain, specifically in amygdala, cerebellum, hippocampus,

cerebral cortex, thalamus and spinal cord (CTs = 30.5-31.9). The GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases.

5   All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and α2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of

10   stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the α-adrenergic receptors have been implicated in memory. Therefore, this gene may be of use as a small molecule target for the treatment of

15   any of the described diseases.

References:

El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

20   1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures,

25   such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine

30   A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having

high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response. The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These

neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

5   The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the

10   possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist.

15   Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A
20   receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal

25   cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, p < 0.05). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, p < 0.05). Neuroprotective properties of SCH

30   58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 1.3D Summary: Ag1570/Ag1733 Two experiments with two different probe and primer sets show highest expression in the spleen and a brain cancer cell line. Thus, expression of this gene could be used to differentiate between these samples and other samples on this panel. There is also low but significant expression in cell lines derived from renal cancer. This is in concordance with the results from panels 2.2 and screening_panel_v1.5. Please see Panel 2.2 for further discussion of potential utility of this gene in kidney cancer.

Panel 2.2 Summary: Ag1570/1733 Expression of the GMAC008745_A gene was assessed in two independent runs on panel 2.2 using two different probe/primer sets. There appears to be good concordance between the runs. The highest expression in both panels appears to be in kidney cancer samples, although they are different samples in the two panels. There is also substantial expression in another sample derived from a kidney cancer. Thus, the expression of this gene could be used to distinguish these kidney cancer samples from other samples in the panel. Moreover, therapeutic modulation of this gene, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of kidney cancer.

Panel 4D Summary: Ag1566/1570/Ag1733 Results from experiments using two different probe/primer sets are in reasonable agreement. The GMAC008745_A gene is most highly expressed in the PMA and ionomycin treated basophil cell line KU-812 and to a lesser extent in untreated KU-812 cells. It is also expressed predominantly in activated B cells and lung fibroblasts treated with IL-4. Therefore, expression of this gene could be used to distinguish these cell types from the other samples on this panel. Basophils play an important role in many allergic diseases and other diseases, such as asthma and inflammatory bowel disease. This gene encodes a putative GPCR and it is known that GPCR-type receptors are important in multiple physiological responses mediated by basophils (ref. 1). Therefore, antibody or small molecule therapies designed with the protein encoded for by this gene could block or inhibit inflammation or tissue damage due to basophil activation in response to asthma, allergies, hypersensitivity reactions, psoriasis, and viral infections. In addition, the expression of this that GPCR-type receptors on activated B cells suggest that antibody or small molecule therapies designed with the protein encoded for by this gene could be beneficial for the treatment of hyperglobulinemia and B cell mediated diseases such as systemic lupus erythematosus, rheumatoid arthritis and Crohn's diseases.

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This transcript is also expressed in TNF-a and IL-1 treated astrocytes. This suggest that antibody or small molecule therapies designed with the protein encoded for by this gene could also be beneficial for the treatment of inflammatory CNS diseases such as multiple sclerosis or stroke.

5   References:

1. Heinemann A., Hartnell A., Stubbs V.E., Murakami K., Soler D., LaRosa G., Askenase P.W., Williams T.J., Sabroe I. (2000) Basophil responses to chemokines are regulated by both sequential and cooperative receptor signaling. J. Immunol. 165: 7224-7233.

To investigate human basophil responses to chemokines, we have developed a sensitive assay
10   that uses flow cytometry to measure leukocyte shape change as a marker of cell responsiveness. PBMC were isolated from the blood of volunteers. Basophils were identified as a single population of cells that stained positive for IL-3Ralpha (CDw123) and negative for HLA-DR, and their increase in forward scatter (as a result of cell shape change) in response to chemokines was measured. Shape change responses of basophils to chemokines
15   were highly reproducible, with a rank order of potency: monocyte chemoattractant protein (MCP) 4 (peak at /= eotaxin-2 = eotaxin-3 >/= eotaxin > MCP-1 = MCP-3 > macrophage-inflammatory protein-1alpha > RANTES = MCP-2 = IL-8. The CCR4-selective ligand macrophage-derived chemokine did not elicit a response at concentrations up to 10 nM. Blocking mAbs to CCR2 and CCR3 demonstrated that responses to higher concentrations
20   (>10 nM) of MCP-1 were mediated by CCR3 rather than CCR2, whereas MCP-4 exhibited a biphasic response consistent with sequential activation of CCR3 at lower concentrations and CCR2 at 10 nM MCP-4 and above. In contrast, responses to MCP-3 were blocked only in the presence of both mAbs, but not after pretreatment with either anti-CCR2 or anti-CCR3 mAb alone. These patterns of receptor usage were different from those seen for eosinophils and
25   monocytes. We suggest that cooperation between CCRs might be a mechanism for preferential recruitment of basophils, as occurs in tissue hypersensitivity responses in vivo.

AU. GMAC002555_B/CG57372-02: Olfactory Receptor

Expression of gene GMAC002555_B (also known as CG57372-02) was assessed
30   using the primer-probe set Ag1731, described in Table AUA. Results of the RTQ-PCR runs are shown in Tables AUB, AUC, AUD, AUE, AUF and AUG.

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Table AUA. Probe Name Ag1731

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atagtgggagagtgggtgagtt-3'	22	26	441
Probe	TET-5'-cctgctcctgcgccactacaggta-3'-TAMRA	24	65	442
Reverse	5'-cagcaaaagggcaaacaatag-3'	21	89	443

Table AUB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag1731, Run 229929906	Tissue Name	Rel. Exp.(%) Ag1731, Run 229929906
AD 1 Hippo	15.7	Control (Path) 3 Temporal Ctx	8.4
AD 2 Hippo	10.5	Control (Path) 4 Temporal Ctx	71.2
AD 3 Hippo	4.2	AD 1 Occipital Ctx	3.5
AD 4 Hippo	3.5	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	100.0	AD 3 Occipital Ctx	0.0
AD 6 Hippo	3.3	AD 4 Occipital Ctx	24.7
Control 2 Hippo	0.7	AD 5 Occipital Ctx	24.3
Control 4 Hippo	9.0	AD 6 Occipital Ctx	15.0
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	0.6
AD 1 Temporal Ctx	0.0	Control 2 Occipital Ctx	25.2
AD 2 Temporal Ctx	19.8	Control 3 Occipital Ctx	21.6
AD 3 Temporal Ctx	0.8	Control 4 Occipital Ctx	2.9
AD 4 Temporal Ctx	22.7	Control (Path) 1 Occipital Ctx	97.9
AD 5 Inf Temporal Ctx	85.9	Control (Path) 2 Occipital Ctx	23.2
AD 5 Sup Temporal Ctx	21.5	Control (Path) 3 Occipital Ctx	1.3
AD 6 Inf Temporal Ctx	27.5	Control (Path) 4 Occipital Ctx	19.6
AD 6 Sup Temporal Ctx	20.3	Control 1 Parietal Ctx	4.1
Control 1 Temporal Ctx	8.2	Control 2 Parietal Ctx	4.5

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Control 2 Temporal Ctx	18.7	Control 3 Parietal Ctx	47.3
Control 3 Temporal Ctx	10.7	Control (Path) 1 Parietal Ctx	65.5
Control 3 Temporal Ctx	11.0	Control (Path) 2 Parietal Ctx	44.1
Control (Path) 1 Temporal Ctx	63.7	Control (Path) 3 Parietal Ctx	0.8
Control (Path) 2 Temporal Ctx	23.5	Control (Path) 4 Parietal Ctx	24.1

Table AUC. General_screening_panel_v1.5

Tissue Name	Rel. Exp.(%) Ag1731, Run 228980732	Tissue Name	Rel. Exp.(%) Ag1731, Run 228980732
Adipose	2.3	Renal ca. TK-10	7.5
Melanoma* Hs688(A).T	9.9	Bladder	18.8
Melanoma* Hs688(B).T	6.7	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	20.7	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	6.3	Colon ca. SW-948	14.1
Melanoma* SK-MEL-5	15.5	Colon ca. SW480	41.8
Squamous cell carcinoma SCC-4	4.0	Colon ca.* (SW480 met) SW620	49.7
Testis Pool	17.1	Colon ca. HT29	24.0
Prostate ca.* (bone met) PC-3	5.5	Colon ca. HCT-116	37.9
Prostate Pool	18.8	Colon ca. CaCo-2	0.0
Placenta	1.3	Colon cancer tissue	7.2
Uterus Pool	13.4	Colon ca. SW1116	1.3
Ovarian ca. OVCAR-3	17.6	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	33.7	Colon ca. SW-48	2.5
Ovarian ca. OVCAR-4	0.0	Colon Pool	11.0
Ovarian ca. OVCAR-5	18.4	Small Intestine Pool	13.4
Ovarian ca. IGROV-1	0.0	Stomach Pool	12.8
Ovarian ca.	9.4	Bone Marrow Pool	1.5

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OVCAR-8			
Ovary	7.0	Fetal Heart	4.2
Breast ca. MCF-7	0.0	Heart Pool	9.1
Breast ca. MDA-MB-231	50.0	Lymph Node Pool	20.2
Breast ca. BT 549	2.7	Fetal Skeletal Muscle	0.8
Breast ca. T47D	0.0	Skeletal Muscle Pool	1.6
Breast ca. MDA-N	33.0	Spleen Pool	0.7
Breast Pool	24.8	Thymus Pool	13.6
Trachea	7.9	CNS cancer (glio/astro) U87-MG	27.0
Lung	9.7	CNS cancer (glio/astro) U-118-MG	5.0
Fetal Lung	6.3	CNS cancer (neuro;met) SK-N-AS	2.7
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	99.3	CNS cancer (astro) SNB-75	3.5
Lung ca. NCI-H146	5.3	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	1.1	CNS cancer (glio) SF-295	31.2
Lung ca. A549	2.2	Brain (Amygdala) Pool	4.3
Lung ca. NCI-H526	1.2	Brain (cerebellum)	3.6
Lung ca. NCI-H23	1.6	Brain (fetal)	30.1
Lung ca. NCI-H460	19.3	Brain (Hippocampus) Pool	17.2
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	21.0
Lung ca. NCI-H522	2.5	Brain (Substantia nigra) Pool	4.2
Liver	0.0	Brain (Thalamus) Pool	27.5
Fetal Liver	6.4	Brain (whole)	24.0
Liver ca. HepG2	0.0	Spinal Cord Pool	0.7
Kidney Pool	10.7	Adrenal Gland	7.1
Fetal Kidney	**100.0**	Pituitary gland Pool	1.7
Renal ca. 786-0	19.1	Salivary Gland	1.5
Renal ca. A498	1.8	Thyroid (female)	0.5
Renal ca. ACHN	5.1	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	5.0	Pancreas Pool	9.9

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Table AUD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1731, Run 165933477	Tissue Name	Rel. Exp.(%) Ag1731, Run 165933477
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	8.2
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	2.8
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	3.1	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	3.5
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	7.7	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	4.0
Brain (thalamus)	7.4	Lung ca. (small cell) NCI-H69	1.6
Cerebral Cortex	5.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	4.9
glio/astro U87-MG	1.2	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	1.4	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	12.2	Breast ca.* (pl.ef)	4.2

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		MDA-MB-231	
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	4.5
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	11.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	1.4	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	15.9
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	5.2	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	4.2
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	2.1	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	3.8	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	4.2
Bladder	7.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table AUE. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag1731, Run 174109700	Tissue Name	Rel. Exp.(%) Ag1731, Run 174109700

Normal Colon	11.6	Kidney Margin (OD04348)	12.2
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	4.9	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	30.8
Colon Margin (OD06159)	5.8	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	12.8
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	27.9	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	13.4	Normal Uterus	12.6
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer 064010	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	13.8	Normal Breast	0.0
Ovarian Margin (OD06283-07)	14.0	Breast Cancer (OD04566)	0.0
Ovarian Cancer 064008	0.0	Breast Cancer 1024	18.2
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis (OD04655-	0.0

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		05)	
Ovarian Margin (OD06455-07)	11.9	Breast Cancer 064006	0.0
Normal Lung	14.4	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	7.4	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	13.5
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	0.0
Lung Cancer (OD05014A)	21.5	Breast cancer node metastasis (OD06083)	14.0
Lung Margin (OD05014B)	13.7	Normal Liver	15.2
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	13.1	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Melanoma Metastasis	0.0	Liver Cancer 6005-T	21.6
Ocular Melanoma Margin (Liver)	20.7	Liver Tissue 6005-N	21.6
Melanoma Metastasis	22.8	Liver Cancer 064003	0.0
Melanoma Margin (Lung)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer 1023	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	12.2	Bladder Cancer A302173	5.5
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	**100.0**	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	5.7
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04340)	11.3	Stomach Margin 9060394	12.3
Kidney Ca, Nuclear	28.3	Gastric Cancer 064005	0.0

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grade 3 (OD04348)			

Table AUF. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag1731, Run 229787985	Tissue Name	Rel. Exp.(%) Ag1731, Run 229787985
Secondary Th1 act	0.3	HUVEC IL-1beta	0.1
Secondary Th2 act	1.4	HUVEC IFN gamma	0.2
Secondary Tr1 act	0.1	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.4
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.1
Primary Th2 act	0.5	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.4	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.2	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.1	Small airway epithelium none	0.1
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.2	Coronery artery SMC TNFalpha + IL-1beta	0.1
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.5
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.4
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.1
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.1
LAK cells IL-2+IL-12	0.0	NCI-H292 none	0.0

LAK cells IL-2+IFN gamma	0.0	NCI-H292 IL-4	1.8
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-9	**100.0**
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-13	0.2
NK Cells IL-2 rest	0.0	NCI-H292 IFN gamma	0.1
Two Way MLR 3 day	0.0	HPAEC none	0.1
Two Way MLR 5 day	0.0	HPAEC TNF alpha + IL-1 beta	0.4
Two Way MLR 7 day	0.0	Lung fibroblast none	0.0
PBMC rest	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.2
PBMC PWM	0.0	Lung fibroblast IL-4	0.1
PBMC PHA-L	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) none	0.4	Lung fibroblast IL-13	0.0
Ramos (B cell) ionomycin	0.6	Lung fibroblast IFN gamma	0.1
B lymphocytes PWM	0.0	Dermal fibroblast CCD1070 rest	0.3
B lymphocytes CD40L and IL-4	0.1	Dermal fibroblast CCD1070 TNF alpha	0.2
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.4
EOL-1 dbcAMP PMA/ionomycin	0.1	Dermal fibroblast IFN gamma	0.0
Dendritic cells none	0.0	Dermal fibroblast IL-4	0.1
Dendritic cells LPS	0.0	Dermal Fibroblasts rest	0.0
Dendritic cells anti-CD40	0.0	Neutrophils TNFa+LPS	0.0
Monocytes rest	0.0	Neutrophils rest	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.1	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.1	Kidney	0.2
HUVEC starved	0.1		

Table AUG. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1731, Run 165812961	Tissue Name	Rel. Exp.(%) Ag1731, Run 165812961
Secondary Th1 act	13.5	HUVEC IL-1beta	10.6
Secondary Th2 act	59.5	HUVEC IFN gamma	5.9

Secondary Tr1 act	56.6	HUVEC TNF alpha + IFN gamma	8.0
Secondary Th1 rest	5.6	HUVEC TNF alpha + IL4	7.7
Secondary Th2 rest	8.8	HUVEC IL-11	6.2
Secondary Tr1 rest	5.0	Lung Microvascular EC none	10.2
Primary Th1 act	38.4	Lung Microvascular EC TNFalpha + IL-1beta	10.8
Primary Th2 act	47.6	Microvascular Dermal EC none	1.3
Primary Tr1 act	48.6	Microsvasular Dermal EC TNFalpha + IL-1beta	3.6
Primary Th1 rest	28.5	Bronchial epithelium TNFalpha + IL1beta	1.1
Primary Th2 rest	11.5	Small airway epithelium none	1.2
Primary Tr1 rest	21.6	Small airway epithelium TNFalpha + IL-1beta	13.5
CD45RA CD4 lymphocyte act	6.3	Coronery artery SMC rest	4.5
CD45RO CD4 lymphocyte act	10.8	Coronery artery SMC TNFalpha + IL-1beta	2.8
CD8 lymphocyte act	6.6	Astrocytes rest	2.5
Secondary CD8 lymphocyte rest	5.7	Astrocytes TNFalpha + IL-1beta	3.2
Secondary CD8 lymphocyte act	12.3	KU-812 (Basophil) rest	2.7
CD4 lymphocyte none	1.9	KU-812 (Basophil) PMA/ionomycin	22.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	11.2	CCD1106 (Keratinocytes) none	14.3
LAK cells rest	1.4	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	39.8
LAK cells IL-2	3.0	Liver cirrhosis	18.9
LAK cells IL-2+IL-12	3.0	Lupus kidney	4.3
LAK cells IL-2+IFN gamma	5.7	NCI-H292 none	26.6
LAK cells IL-2+ IL-18	4.2	NCI-H292 IL-4	32.8
LAK cells PMA/ionomycin	1.4	NCI-H292 IL-9	30.6
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	11.4
Two Way MLR 3 day	2.2	NCI-H292 IFN gamma	8.5
Two Way MLR 5 day	1.8	HPAEC none	9.0

Two Way MLR 7 day	6.5	HPAEC TNF alpha + IL-1 beta	10.3
PBMC rest	1.3	Lung fibroblast none	5.6
PBMC PWM	3.2	Lung fibroblast TNF alpha + IL-1 beta	5.9
PBMC PHA-L	15.7	Lung fibroblast IL-4	10.7
Ramos (B cell) none	**100.0**	Lung fibroblast IL-9	9.7
Ramos (B cell) ionomycin	47.0	Lung fibroblast IL-13	4.5
B lymphocytes PWM	0.9	Lung fibroblast IFN gamma	6.0
B lymphocytes CD40L and IL-4	6.0	Dermal fibroblast CCD1070 rest	35.1
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	26.2
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	15.5
Dendritic cells none	1.8	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	1.4
Dendritic cells anti-CD40	2.5	IBD Colitis 2	2.1
Monocytes rest	0.0	IBD Crohn's	1.0
Monocytes LPS	0.0	Colon	20.2
Macrophages rest	7.9	Lung	1.2
Macrophages LPS	0.0	Thymus	2.9
HUVEC none	20.3	Kidney	17.4
HUVEC starved	20.7		

CNS_neurodegeneration_v1.0 Summary: Ag1731 No difference was detected in the expression of this gene in the postmortem brains of Alzheimer's diseased patients when compared to controls; however this panel demonstrates the expression of this gene in the brains of an independent group of subjects. See panel 1.3d for additional discussion of the potential utility of this gene in the central nervous system.

General_screening_panel_v1.5 Summary: Ag1731 Expression of the GMAC002555_B gene is highest in a sample derived from fetal kidney tissue (CT = 30.2). Of note is the absence of expression of this gene in the sample of adult kidney tissue. Thus, the expression of this gene could be used to distinguish fetal kidney tissue from adult kidney tissue as well as from the other samples in the panel. In addition, there is substantial expression of this gene

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in a number of samples including a lung cancer cell line, breast cancer cell lines and a cluster of colon cancer cell lines. Therefore, therapeutic modulation of this gene, through the use of antibodies, small molecule drugs or protein therapeutics might be of benefit in the treatment of colon cancer, lung cancer or breast cancer.

5   This gene represents a novel G-protein coupled receptor (GPCR) that also shows expression in the brain. The GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics

10   have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and $\alpha 2$ adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate

15   receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the α-adrenergic receptors have been implicated in memory. Therefore this gene may be of use as a small molecule target for the treatment of any of the described

20   diseases.

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

25   1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures,

30   such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to

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'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was

5   confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced

10   the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A

15   receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry
20   2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per

25   action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response.

30   The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated

excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a

5   mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

10   The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor

15   channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist.

20   Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A
25   receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9 Related Articles, Books, LinkOut

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal

30   cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, $p < 0.05$). Similar

effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, $p < 0.05$). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 1.3D Summary: Ag1731 Expression of the GMAC002555_B gene is only expressed in the spleen (CT = 32.9), an important site of secondary immune responses. Therefore, expression of this gene can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: Ag1731 Significant expression of the GMAC002555_B gene is seen exclusively in a kidney cancer sample (CT = 34.3). Interestingly, expression of this gene is much higher in the kidney cancer sample when compared to the adjacent matched normal tissue. Therefore, expression of this gene may be used to distinguish kidney cancer from normal kidney. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene, using small molecule drugs or antibodies, may be beneficial in the treatment of kidney cancer.

Panel 4.1D Summary: Ag1731 Data from one experiment with this probe and primer set is not included, because the amp plot indicates that there were experimental difficulties with this run (data not shown).

Panel 4D Summary: Ag 1731 The GMAC002555_B gene is expressed at low to moderate levels in a number of samples on this panel. Expression of this gene is highest in a Ramos B lymphoma cell line (CT = 30) with moderate expression also seen in activated Th2 and regulatory Tr1 T cells and activated Th1 cells. In addition, this transcript is found in spleen, an important site of secondary immune responses, which is consistent with the expression in activated T cells. This observation is consistent with what is observed in Panel 1.3D. Therefore, small molecule or antibody therapeutics designed against the GPCR encoded for by this gene could be utilized to modulate function of activated T cells and treat patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, rheumatoid arthritis and psoriasis.

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AV. GMAC002555_A: GPCR

Expression of gene GMAC002555_A was assessed using the primer-probe sets Ag2483 and Ag1729, described in Tables AVA and AVB. Results of the RTQ-PCR runs are shown in Tables AVC, AVD and AVE.

Table AVA. Probe Name Ag2483

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gtgaatttgttctcgtgagctt-3'	22	30	444
Probe	TET-5'-ccctgtccactgagcttcaggctcta-3'-TAMRA	26	57	445
Reverse	5'-tggtcaagaaaaggagaaacag-3'	22	83	446

Table AVB. Probe Name Ag1729

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atttgttctcgtgagcttctca-3'	22	34	447
Probe	TET-5'-ccctgtccactgagcttcaggctcta-3'-TAMRA	26	57	448
Reverse	5'-cattgcccattaaagtaaccaa-3'	22	110	449

Table AVC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2483, Run 208777958	Tissue Name	Rel. Exp.(%) Ag2483, Run 208777958
AD 1 Hippo	9.4	Control (Path) 3 Temporal Ctx	10.6
AD 2 Hippo	15.1	Control (Path) 4 Temporal Ctx	20.7
AD 3 Hippo	5.0	AD 1 Occipital Ctx	15.3
AD 4 Hippo	23.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	90.8	AD 3 Occipital Ctx	0.0
AD 6 Hippo	23.2	AD 4 Occipital Ctx	14.9
Control 2 Hippo	12.2	AD 5 Occipital Ctx	11.2
Control 4 Hippo	2.5	AD 6 Occipital Ctx	11.7
Control (Path) 3 Hippo	14.1	Control 1 Occipital Ctx	2.1
AD 1 Temporal Ctx	2.9	Control 2 Occipital	22.8

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		Ctx	.
AD 2 Temporal Ctx	18.4	Control 3 Occipital Ctx	29.9
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	17.9	Control (Path) 1 Occipital Ctx	84.1
AD 5 Inf Temporal Ctx	39.8	Control (Path) 2 Occipital Ctx	29.5
AD 5 Sup Temporal Ctx	21.9	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	14.8	Control (Path) 4 Occipital Ctx	50.7
AD 6 Sup Temporal Ctx	22.2	Control 1 Parietal Ctx	13.7
Control 1 Temporal Ctx	9.3	Control 2 Parietal Ctx	32.1
Control 2 Temporal Ctx	9.8	Control 3 Parietal Ctx	16.5
Control 3 Temporal Ctx	20.2	Control (Path) 1 Parietal Ctx	70.2
Control 3 Temporal Ctx	18.7	Control (Path) 2 Parietal Ctx	36.6
Control (Path) 1 Temporal Ctx	**100.0**	Control (Path) 3 Parietal Ctx	8.0
Control (Path) 2 Temporal Ctx	78.5	Control (Path) 4 Parietal Ctx	85.9

Table AVD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2483, Run 165639504	Tissue Name	Rel. Exp.(%) Ag2483, Run 165639504
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	65.5	Renal ca. 786-0	34.4
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	18.2
Adrenal gland	37.1	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	19.5	Liver	0.0
Brain (whole)	74.2	Liver (fetal)	0.0

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Brain (amygdala)	12.9	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	40.1	Lung	55.1
Brain (hippocampus)	10.0	Lung (fetal)	0.0
Brain (substantia nigra)	50.0	Lung ca. (small cell) LX-1	86.5
Brain (thalamus)	18.6	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	37.4	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	17.7
glio/astro U87-MG	36.9	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	37.6	Lung ca. (non-s.cell) NCI-H23	46.0
astrocytoma SW1783	69.7	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	22.2
astrocytoma SNB-75	44.1	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	39.0
Glioma U251	34.9	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	53.2	Breast ca.* (pl.ef) MDA-MB-231	**100.0**
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	41.8	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	15.1
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	14.8	Ovarian ca. OVCAR-3	0.0
Thymus	33.2	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	21.3
Lymph node	83.5	Ovarian ca. OVCAR-8	31.4
Colorectal	32.1	Ovarian ca. IGROV-1	0.0

Stomach	21.6	Ovarian ca.* (ascites) SK-OV-3	52.5
Small intestine	45.4	Uterus	4.9
Colon ca. SW480	57.4	Plancenta	84.1
Colon ca.* SW620(SW480 met)	37.4	Prostate	0.0
Colon ca. HT29	22.2	Prostate ca.* (bone met)PC-3	17.2
Colon ca. HCT-116	46.0	Testis	80.7
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	7.1	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	40.1
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	13.7
Bladder	47.3	Melanoma LOX IMVI	0.0
Trachea	20.2	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table AVE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1729, Run 165767258	Rel. Exp.(%) Ag2483, Run 164391871	Tissue Name	Rel. Exp.(%) Ag1729, Run 165767258	Rel. Exp.(%) Ag2483, Run 164391871
Secondary Th1 act	11.9	7.1	HUVEC IL-1beta	20.3	2.4
Secondary Th2 act	97.9	30.8	HUVEC IFN gamma	14.3	6.8
Secondary Tr1 act	**100.0**	19.6	HUVEC TNF alpha + IFN gamma	4.9	5.0
Secondary Th1 rest	5.5	0.0	HUVEC TNF alpha + IL4	12.0	7.7
Secondary Th2 rest	4.0	3.2	HUVEC IL-11	8.5	1.9
Secondary Tr1 rest	7.4	1.5	Lung Microvascular EC none	13.3	9.6
Primary Th1 act	41.2	18.6	Lung Microvascular EC	9.7	6.9

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			TNFalpha + IL-1beta		
Primary Th2 act	48.0	7.9	Microvascular Dermal EC none	3.6	1.2
Primary Tr1 act	91.4	13.9	Microsvasular Dermal EC TNFalpha + IL-1beta	3.8	1.0
Primary Th1 rest	28.9	9.3	Bronchial epithelium TNFalpha + IL1beta	2.2	1.9
Primary Th2 rest	12.4	2.2	Small airway epithelium none	0.0	0.7
Primary Tr1 rest	13.5	5.3	Small airway epithelium TNFalpha + IL-1beta	18.8	15.1
CD45RA CD4 lymphocyte act	8.8	2.5	Coronery artery SMC rest	8.4	3.0
CD45RO CD4 lymphocyte act	17.4	7.3	Coronery artery SMC TNFalpha + IL-1beta	3.2	3.7
CD8 lymphocyte act	10.4	3.8	Astrocytes rest	5.1	0.0
Secondary CD8 lymphocyte rest	5.2	1.9	Astrocytes TNFalpha + IL-1beta	6.6	1.9
Secondary CD8 lymphocyte act	13.4	5.4	KU-812 (Basophil) rest	10.2	2.7
CD4 lymphocyte none	0.8	0.5	KU-812 (Basophil) PMA/ionomycin	26.6	11.1
2ry Th1/Th2/Tr1_anti-CD95 CH11	8.4	3.4	CCD1106 (Keratinocytes) none	7.4	7.5
LAK cells rest	1.7	1.6	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	37.4	0.0
LAK cells IL-2	3.4	1.0	Liver cirrhosis	29.7	4.8
LAK cells IL-2+IL-12	3.9	0.7	Lupus kidney	3.3	1.7
LAK cells IL-2+IFN gamma	5.3	0.9	NCI-H292 none	54.7	25.2

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LAK cells IL-2+ IL-18	0.6	1.2	NCI-H292 IL-4	55.9	23.3
LAK cells PMA/ionomycin	4.2	1.7	NCI-H292 IL-9	66.0	22.2
NK Cells IL-2 rest	1.5	0.4	NCI-H292 IL-13	32.1	8.3
Two Way MLR 3 day	0.0	0.6	NCI-H292 IFN gamma	29.3	15.0
Two Way MLR 5 day	2.4	1.0	HPAEC none	11.1	6.2
Two Way MLR 7 day	5.0	1.5	HPAEC TNF alpha + IL-1 beta	18.2	7.5
PBMC rest	2.8	0.9	Lung fibroblast none	6.2	3.0
PBMC PWM	0.6	3.1	Lung fibroblast TNF alpha + IL-1 beta	8.7	1.1
PBMC PHA-L	5.3	8.2	Lung fibroblast IL-4	2.8	1.9
Ramos (B cell) none	94.6	33.4	Lung fibroblast IL-9	9.9	4.0
Ramos (B cell) ionomycin	72.7	**100.0**	Lung fibroblast IL-13	8.9	1.4
B lymphocytes PWM	0.8	2.1	Lung fibroblast IFN gamma	6.3	1.9
B lymphocytes CD40L and IL-4	3.6	0.8	Dermal fibroblast CCD1070 rest	57.8	14.5
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	52.5	30.6
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	21.0	12.3
Dendritic cells none	0.0	0.6	Dermal fibroblast IFN gamma	0.0	1.9
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.7	1.6
Dendritic cells anti-CD40	0.0	1.0	IBD Colitis 2	3.6	2.6
Monocytes rest	0.0	0.0	IBD Crohn's	2.5	0.8
Monocytes LPS	0.0	0.0	Colon	19.8	6.1
Macrophages rest	11.5	4.0	Lung	1.7	0.9
Macrophages LPS	0.7	0.0	Thymus	9.0	7.3
HUVEC none	25.9	6.9	Kidney	8.0	7.7
HUVEC starved	55.9	15.1			

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CNS_neurodegeneration_v1.0 Summary: Ag2483 The protein encoded by the GMAC002555_A gene contains homology to the GPCR family of receptors, and is shown by panel CNS_Neurodegeneration_V1.0 to be expressed in the brain, with gene expression down regulated in the temporal cortex of the Alzheimer's diseased brain. The temporal cortex is a region that specifically shows neurodegeneration in Alzheimer's disease. Several neurotransmitter receptors are GPCRs, including the dopamine receptor family, the serotonin receptor family, the GABAB receptor, and the muscarinic acetylcholine receptors. Thus, the GPCR encoded by the GMAC002555_A gene may represent a novel neurotransmitter receptor. Targeting various neurotransmitter receptors, such as dopamine, serotonin receptors, has proven to be an effective therapy in psychiatric illnesses such as schizophrenia, bipolar disorder and depression. Furthermore the cerebral cortex and hippocampus are regions of the brain that are known to play critical roles in Alzheimer's disease, seizure disorders, and in the normal process of memory formation. Thus, therapeutic modulation of this gene or its protein product may be beneficial in one or more of these diseases, as may stimulation of the receptor coded for by the gene.

Panel 1.3D Summary: Ag2483 Significant expression of the GMAC002555_A gene is limited to a sample derived from a breast cancer cell line (CT=34.9). Thus, the expression of this gene could be used to distinguish this cell line from other samples. Furthermore, therapeutic modulation of the expression or function of the protein encoded by the GMAC002555_A gene, through the use of small molecule drugs or antibodies, might be beneficial in the treatment of breast cancer.

Panel 4D Summary: Ag2483/Ag1729 Two experiments using two different probe and primer sets show highest expression of the GMAC002555_A gene in ionomycin-activated Ramos B lymphblastoid cells (CT=29.4) in one run and in activated Tr1 cells (CT=32.2) in the second run. Moderate expression is also detected in activated Th1 and Th2 cells, resting and cytokine-activated dermal fibroblasts, and in resting and cytokine activated mucoepidermoid cells. Inhibition of the function of the protein encoded by the GMAC002555_A gene by a specific antibody or small molecule drug may reduce inflammation and autoimmunity that result from asthma, psoriasis, and inflammatory bowel disease.

AW. GMAC005255_A: GPCR

Expression of gene GMAC005255_A was assessed using the primer-probe set Ag1721, described in Table AWA. Results of the RTQ-PCR runs are shown in Table AWB.

Table AWA. Probe Name Ag1721

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ccatgtacttcttcctctccaa-3'	22	173	450
Probe	TET-5'-tcagttttgtgtctaccactgtcccg-3'-TAMRA	26	212	451
Reverse	5'-tctggatattcaccagcatctt-3'	22	238	452

Table AWB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1721, Run 165767703	Tissue Name	Rel. Exp.(%) Ag1721, Run 165767703
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	2.3	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	2.4
CD8 lymphocyte act	0.0	Astrocytes rest	0.0

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Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	2.4
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.8	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	1.1	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.5
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.9
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	2.3
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.6
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	1.5	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	3.3	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	4.7
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	19.3
Monocytes rest	0.0	IBD Crohn's	0.5

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Monocytes LPS	2.4	Colon	4.6
Macrophages rest	0.0	Lung	3.2
Macrophages LPS	0.0	Thymus	1.7
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 4D Summary: <u>Ag1721</u> Significant expression of the GMAC005255_A gene is detected only in a liver cirrhosis sample (CT = 31.2). This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

AX. GMAC002988_A: GPCR

Expression of gene GMAC002988_A was assessed using the primer-probe set Ag1720, described in Table AXA. Results of the RTQ-PCR runs are shown in Table AXB.

<u>Table AXA</u>. Probe Name Ag1720

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-agggaatgagacacaaatttca-3'	22	9	453
Probe	TET-5'-acaagaattgcagcccttcctctttg-3'-TAMRA	26	60	454
Reverse	5'-caggtacatggacaggaacag-3'	21	88	455

<u>Table AXB</u>. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag1720, Run 173761687	Tissue Name	Rel. Exp.(%) Ag1720, Run 173761687
Normal Colon	0.0	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin	1.1	Kidney Margin	0.0

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(OD06159)		(OD04450-03)	
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	1.2	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	0.0
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer 064010	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer (OD04566)	0.0
Ovarian Cancer 064008	**100.0**	Breast Cancer 1024	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis (OD04655-05)	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer 064006	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer	0.0	Breast Margin	9.3

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(OD03126)		A2090734	
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	7.9
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	0.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	26.6
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	5.3	Liver Tissue 6004-N	0.0
Ocular Melanoma Metastasis	0.0	Liver Cancer 6005-T	0.0
Ocular Melanoma Margin (Liver)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer 064003	0.0
Melanoma Margin (Lung)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer 1023	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	5.5	Bladder Cancer A302173	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade ½ (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Panel 1.3D Summary: Ag1720 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag1720 Expression of the GMAC002988_A gene is highest in an ovarian cancer sample (CT = 32.6). This gene is also expressed at low but significant levels in a liver cancer sample (CT = 34.5). Therefore, expression of this gene may be used to

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distinguish ovarian and liver cancers from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of ovarian and liver cancer.

Panel 4D Summary: <u>Ag1720</u> Expression of this gene is low/undetectable (CTs > 34.5)
5   across all of the samples on this panel (data not shown).

AY. GMAC006271_B: GPCR

Expression of gene GMAC006271_B was assessed using the primer-probe set Ag1719, described in Table AYA. Results of the RTQ-PCR runs are shown in Table AYB.

10   <u>Table AYA</u>. Probe Name Ag1719

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tggcttcagtgatgtacactgt-3'	22	669	456
Probe	TET-5'-cccatgctgaacccttcatctacag-3'-TAMRA	26	698	457
Reverse	5'-cactttgaatgtccttgttcct-3'	22	728	458

<u>Table AYB</u>. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1719, Run 165767672	Tissue Name	Rel. Exp.(%) Ag1719, Run 165767672
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	4.2	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0

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Primary Th1 rest	0.7	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L	0.0	Dermal fibroblast	0.0

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and IL-4		CCD1070 rest	
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	6.1
Dendritic cells anti-CD40	0.0	IBD Colitis 2	3.5
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	1.6
Macrophages LPS	2.6	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 4D Summary: Ag1719 Significant expression of the GMAC006271_B gene is detected in a liver cirrhosis sample (CT = 32.8). This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

AZ. GMAC023080_A: GPCR

Expression of gene GMAC023080_A was assessed using the primer-probe set Ag1713, described in Table AZA. Results of the RTQ-PCR runs are shown in Table AZB.

Table AZA. Probe Name Ag1713

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tcattgaccatttcatctgtga-3'	22	605	459
Probe	TET-5'-ccctctgctaaaactctcctgcactga-3'-TAMRA	27	633	460
Reverse	5'-caaagagtccaaagacgtgagt-3'	22	661	461

Table AZB. Panel 4D

Tissue Name	Rel. Exp.(%)	Tissue Name	Rel. Exp.(%)

	Ag1713, Run 165768303		Ag1713, Run 165768303
Secondary Th1 act	3.2	HUVEC IL-1beta	0.0
Secondary Th2 act	3.5	HUVEC IFN gamma	0.0
Secondary Tr1 act	4.6	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	2.1	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	7.6	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells	0.0	NCI-H292 IL-9	0.0

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PMA/ionomycin			
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	6.5	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	2.6	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	62.0
Monocytes rest	0.0	IBD Crohn's	17.6
Monocytes LPS	0.0	Colon	2.6
Macrophages rest	0.0	Lung	7.6
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 4D Summary: <u>Ag1713</u> Highest expression of the GMAC023080_A gene is seen in liver cirrhosis (CT=34.1). Furthermore, no expression in normal liver is seen in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

Low but significant expression is also seen in a sample derived from a patient with IBD colitis, but not in normal colon. This observation suggests that the protein encoded by

this gene may be involved in the inflammatory bowel disease process. Therefore, therapeutic modulation of the expression or function of this gene product could potentially be useful in treating the symptoms of this disease.

5   **BA. GMAC022891_A: GPCR**

Expression of gene GMAC022891_A was assessed using the primer-probe set Ag1712, described in Table BAA. Results of the RTQ-PCR runs are shown in Table BAB.

Table BAA. Probe Name Ag1712

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-attccattgctcttccaactct-3'	22	549	462
Probe	TET-5'-cctgttccaacacccaacacagtaaga-3'-TAMRA	27	571	463
Reverse	5'-ttgctccagaaaggacagtaaa-3'	22	603	464

Table BAB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1712, Run 165330417	Tissue Name	Rel. Exp.(%) Ag1712, Run 165330417
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	11.2
Primary Th1 act	7.5	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium	2.5

		TNFalpha + IL-1beta	
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	23.3
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	11.3	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	**100.0**
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0

Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	6.0
Monocytes rest	0.0	IBD Crohn's	5.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	4.5
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 4D Summary: Ag1712 The GMAC022891_A gene is expressed only in pulmonary artery endothelial cells treated with the inflammatory cytokines TNF-a and IL-1. Therefore, expression of this gene could be used to distinguish these cells from the other samples on this panel. This gene encodes a putative GPCR and it is known that GPCR-type receptors are

5 important in multiple physiological responses mediated by endothelial cells and, in particular, in chemotaxis (references 1 and 2). Therefore, small molecule therapeutics or antibody therapeutics designed against the GPCR encoded for by this gene could be utilized in the migration of leukocytes to the lung tissues and to prevent inflammatory lung diseases such asthma, emphysema or bronchitis.

10 References:

1- Takada Y, Kato C, Kondo S, Korenaga R, Ando J. Cloning of cDNAs encoding G protein-coupled receptor expressed in human endothelial cells exposed to fluid shear stress. Biochem Biophys Res Commun 1997 Nov 26;240(3):737-41

A cDNA library of human umbilical vein endothelial cells exposed to fluid shear stress was

15 constructed to search for functional endothelial genes expressed under flow conditions, and cDNAs encoding members of the G protein-coupled receptor (GPCR) family were cloned by a polymerase chain reaction (PCR) method using degenerate oligonucleotide primers. One of the two GPCR clones obtained was edg-1, and the other clone is a novel gene named FEG-1 that encodes a 375-amino acid protein similar to the receptors for both angiotensin II and

20 chemokines. Reverse transcriptase-PCR showed that the FEG-1 and edg-1 mRNA levels in endothelial cells increased markedly in response to fluid flow. This suggests that FEG-1 and edg-1 may be receptor genes that play important roles in the regulation of endothelial function under physiological blood flow conditions

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2- Lee MJ, Thangada S, Paik JH, Sapkota GP, Ancellin N, Chae SS, Wu M, Morales-Ruiz M, Sessa WC, Alessi DR, Hla T. Akt-mediated phosphorylation of the G protein-coupled receptor EDG-1 is required for endothelial cell chemotaxis. Mol Cell 2001 Sep;8(3):693-704

The role of the protein kinase Akt in cell migration is incompletely understood. Here we show that sphingosine-1-phosphate (S1P)-induced endothelial cell migration requires the Akt-mediated phosphorylation of the G protein-coupled receptor (GPCR) EDG-1. Activated Akt binds to EDG-1 and phosphorylates the third intracellular loop at the T(236) residue. Transactivation of EDG-1 by Akt is not required for G(i)-dependent signaling but is indispensable for Rac activation, cortical actin assembly, and chemotaxis. Indeed, T236AEDG-1 mutant sequestered Akt and acted as a dominant-negative GPCR to inhibit S1P-induced Rac activation, chemotaxis, and angiogenesis. Transactivation of GPCRs by Akt may constitute a specificity switch to integrate rapid G protein-dependent signals into long-term cellular phenomena such as cell migration.

BB. GMAC022289_B: GPCR

Expression of gene GMAC022289_B was assessed using the primer-probe set Ag1710, described in Table BBA. Results of the RTQ-PCR runs are shown in Tables BBB, BBC and BBD.

Table BBA. Probe Name Ag1710

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ttgggcttctcagaatttcc-3'	20	68	465
Probe	TET-5'-cctgttcctggtcttcctgaccatct-3'-TAMRA	26	103	466
Reverse	5'-ttccccatcacagtgattgt-3'	20	131	467

Table BBB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1710, Run 165925624	Tissue Name	Rel. Exp.(%) Ag1710, Run 165925624
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0

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Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca.	0.0

		OVCAR-4	
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	12.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	18.9	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	2.4
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table BBC. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag1710, Run 173761451	Tissue Name	Rel. Exp.(%) Ag1710, Run 173761451
Normal Colon	0.0	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin	0.0	Kidney Margin	0.0

(OD06159)		(OD04450-03)	
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	0.0
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer 064010	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer (OD04566)	13.3
Ovarian Cancer 064008	**100.0**	Breast Cancer 1024	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	16.7	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis (OD04655-05)	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer 064006	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer	0.0	Breast Margin	0.0

(OD03126)		A2090734	
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	0.0
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	0.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.0	Liver Tissue 6004-N	0.0
Ocular Melanoma Metastasis	0.0	Liver Cancer 6005-T	14.0
Ocular Melanoma Margin (Liver)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer 064003	0.0
Melanoma Margin (Lung)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer 1023	12.5
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer A302173	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade ½ (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	14.3
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	41.5
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table BBD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1710, Run 165814099	Tissue Name	Rel. Exp.(%) Ag1710, Run 165814099
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0

Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	7.7	Lung Microvascular EC TNFalpha + IL-1beta	5.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0

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Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	15.3
Monocytes rest	0.0	IBD Crohn's	2.5
Monocytes LPS	0.0	Colon	8.4
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: <u>Ag1710</u> Expression of the GMAC022289_B gene is restricted to the spleen, an important site of secondary immune responses (CT = 33.8). Therefore, expression of this gene can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: <u>Ag1710</u> Significant expression of the GMAC022289_B gene is seen exclusively in an ovarian cancer sample (CT = 34.2). Therefore, expression of this gene may be used to distinguish ovarian cancers from the other samples on this panel. Furthermore,

therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of ovarian cancer.

Panel 4D Summary: Ag1710 Highest expression of the GMAC022289_B gene is seen in liver cirrhosis (CT = 34.4) with lower expression in the colon. Furthermore, no expression in normal liver is seen in Panels 1.3D and 2.2, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

BC. GMAC022289_A: GPCR

Expression of gene GMAC022289_A was assessed using the primer-probe set Ag1709, described in Table BCA. Results of the RTQ-PCR runs are shown in Tables BCB and BCC.

Table BCA. Probe Name Ag1709

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gctattctttcttgccaccttt-3'	22	599	468
Probe	TET-5'-tcagcacactactcatcgttctcaca-3'-TAMRA	26	628	469
Reverse	5'-tggttacaacaatgaacgcata-3'	22	657	470

Table BCB. General_screening_panel_v1.5

Tissue Name	Rel. Exp.(%) Ag1709, Run 228980730	Tissue Name	Rel. Exp.(%) Ag1709, Run 228980730
Adipose	70.2	Renal ca. TK-10	1.2
Melanoma* Hs688(A).T	0.8	Bladder	2.6
Melanoma* Hs688(B).T	1.0	Gastric ca. (liver met.) NCI-N87	1.2
Melanoma* M14	0.9	Gastric ca. KATO III	1.9
Melanoma* LOXIMVI	0.5	Colon ca. SW-948	2.0
Melanoma* SK-MEL-5	0.1	Colon ca. SW480	1.9
Squamous cell	0.7	Colon ca.* (SW480	1.9

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carcinoma SCC-4		met) SW620	
Testis Pool	3.3	Colon ca. HT29	0.9
Prostate ca.* (bone met) PC-3	15.1	Colon ca. HCT-116	0.8
Prostate Pool	1.6	Colon ca. CaCo-2	1.0
Placenta	2.2	Colon cancer tissue	0.9
Uterus Pool	0.9	Colon ca. SW1116	0.7
Ovarian ca. OVCAR-3	2.0	Colon ca. Colo-205	1.3
Ovarian ca. SK-OV-3	2.9	Colon ca. SW-48	1.0
Ovarian ca. OVCAR-4	1.8	Colon Pool	8.6
Ovarian ca. OVCAR-5	1.7	Small Intestine Pool	0.9
Ovarian ca. IGROV-1	4.2	Stomach Pool	**100.0**
Ovarian ca. OVCAR-8	1.4	Bone Marrow Pool	2.2
Ovary	1.9	Fetal Heart	1.0
Breast ca. MCF-7	2.0	Heart Pool	2.0
Breast ca. MDA-MB-231	2.8	Lymph Node Pool	0.7
Breast ca. BT 549	2.1	Fetal Skeletal Muscle	1.7
Breast ca. T47D	1.4	Skeletal Muscle Pool	0.7
Breast ca. MDA-N	0.6	Spleen Pool	1.0
Breast Pool	1.6	Thymus Pool	1.5
Trachea	1.2	CNS cancer (glio/astro) U87-MG	2.0
Lung	0.9	CNS cancer (glio/astro) U-118-MG	2.0
Fetal Lung	1.3	CNS cancer (neuro;met) SK-N-AS	0.8
Lung ca. NCI-N417	1.0	CNS cancer (astro) SF-539	2.3
Lung ca. LX-1	3.8	CNS cancer (astro) SNB-75	1.7
Lung ca. NCI-H146	0.5	CNS cancer (glio) SNB-19	1.1
Lung ca. SHP-77	0.5	CNS cancer (glio) SF-295	1.1
Lung ca. A549	0.5	Brain (Amygdala) Pool	1.7
Lung ca. NCI-H526	1.1	Brain (cerebellum)	1.8

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Lung ca. NCI-H23	1.9	Brain (fetal)	2.1
Lung ca. NCI-H460	0.2	Brain (Hippocampus) Pool	1.4
Lung ca. HOP-62	3.2	Cerebral Cortex Pool	2.1
Lung ca. NCI-H522	4.1	Brain (Substantia nigra) Pool	1.8
Liver	1.1	Brain (Thalamus) Pool	2.7
Fetal Liver	1.9	Brain (whole)	1.7
Liver ca. HepG2	0.6	Spinal Cord Pool	2.5
Kidney Pool	1.1	Adrenal Gland	1.7
Fetal Kidney	3.5	Pituitary gland Pool	2.8
Renal ca. 786-0	0.5	Salivary Gland	2.9
Renal ca. A498	1.9	Thyroid (female)	2.2
Renal ca. ACHN	25.7	Pancreatic ca. CAPAN2	1.4
Renal ca. UO-31	4.8	Pancreas Pool	1.4

Table BCC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1709, Run 165768294	Tissue Name	Rel. Exp.(%) Ag1709, Run 165768294
Secondary Th1 act	0.0	HUVEC IL-1beta	3.7
Secondary Th2 act	4.3	HUVEC IFN gamma	0.0
Secondary Tr1 act	9.7	HUVEC TNF alpha + IFN gamma	3.3
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	3.6	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	18.8
Primary Tr1 rest	1.9	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4	0.0	Coronery artery SMC rest	0.0

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lymphocyte act			
CD45RO CD4 lymphocyte act	10.7	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	6.9	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	13.6	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	4.9
CD4 lymphocyte none	11.1	KU-812 (Basophil) PMA/ionomycin	5.1
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	8.9	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	6.4
Two Way MLR 3 day	8.7	NCI-H292 IFN gamma	4.5
Two Way MLR 5 day	5.7	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	9.7	Lung fibroblast none	8.2
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	7.5	Lung fibroblast IL-4	6.1
Ramos (B cell) none	3.6	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	3.7	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	18.4
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	10.0
Dendritic cells none	5.9	Dermal fibroblast IFN gamma	0.0

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Dendritic cells LPS	3.7	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	58.6
Monocytes rest	0.0	IBD Crohn's	13.6
Monocytes LPS	0.0	Colon	11.2
Macrophages rest	0.0	Lung	7.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

General_screening_panel_v1.5 Summary: Ag1709 Expression of the GMAC022289_A gene is highest in a sample derived from normal stomach (CT = 27.5). In addition, there is substantial expression of this gene in samples derived from normal colon tissue and adipose tissue, as well as a renal cell cancer cell line (ACHN). In the majority of other samples, expression was much lower. Thus, the expression of this gene could be used to distinguish the above listed samples from the other samples in this panel. Furthermore, the high expression detected in adipose may suggest that this gene plays an important role in metabolic diseases, including diabetes and obesity.

This gene represents a novel G-protein coupled receptor (GPCR) and also shows low levels of expression in the brain, including in the amygdala, cerebellum, hippocampus, cerebral cortex, substantia nigra, and thalamus. The GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine, muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and α2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the α-adrenergic receptors have been implicated in memory. Therefore, this

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gene may be of use as a small molecule target for the treatment of any of the described diseases.

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response. The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis.

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NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9 Related Articles, Books, LinkOut

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, $p < 0.05$). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, $p < 0.05$). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 4D Summary: Ag1709 Expression of the GMAC022289_A gene is restricted to liver cirrhosis and IBD Colitis (CTs = 33-34). The function of the putative GPCR encoded by this gene may thus be important in the disease processes in both inflammatory bowel disease and in liver cirrhosis. Therefore, blocking antibodies or small molecule antagonists targeted to this GPCR may be useful as therapeutics in colitis and in cirrhosis.

BD. GMAC009594_C and CG50297_01: GPCR

Expression of gene GMAC009594_C and variant CG50297_01 was assessed using the primer-probe sets Ag1851, Ag2544 and Ag1706, described in Tables BDA, BDB and BDC. Results of the RTQ-PCR runs are shown in Tables BDD, BDE, BDF and BDG.

Table BDA. Probe Name Ag1851

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ttaattgtgctgagggaagaaa-3'	22	688	471
Probe	TET-5'-cttctctacctgttcagcgcactcga-3'-TAMRA	26	716	472
Reverse	5'-aagggctgaaccgtagaataag-3'	22	752	473

Table BDB. Probe Name Ag2544

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ttattctacggttcagcccttt-3'	22	753	474
Probe	TET-5'-tgtacatgaaacccaagtcaaagaaca-3'-TAMRA	27	778	475
Reverse	5'-cactccataagacagcccaata-3'	22	824	476

Table BDC. Probe Name Ag1706

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ttaattgtgctgagggaagaaa-3'	22	688	477
Probe	TET-5'-cttctctacctgttcagcgcactcga-3'-TAMRA	26	716	478
Reverse	5'-aagggctgaaccgtagaataag-3'	22	752	479

Table BDD. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag1851, Run 207926307	Rel. Exp.(%) Ag2544, Run 206974241	Tissue Name	Rel. Exp.(%) Ag1851, Run 207926307	Rel. Exp.(%) Ag2544, Run 206974241
AD 1 Hippo	14.1	16.3	Control (Path) 3 Temporal Ctx	2.1	14.0
AD 2 Hippo	57.4	35.6	Control (Path) 4 Temporal Ctx	55.9	34.2
AD 3 Hippo	12.3	9.9	AD 1 Occipital Ctx	24.3	13.0
AD 4 Hippo	8.6	18.9	AD 2 Occipital Ctx (Missing)	0.0	0.0
AD 5 hippo	56.6	28.1	AD 3 Occipital Ctx	7.6	10.0

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AD 6 Hippo	54.3	87.7	AD 4 Occipital Ctx	45.1	33.2
Control 2 Hippo	16.8	33.4	AD 5 Occipital Ctx	8.5	8.1
Control 4 Hippo	21.2	20.4	AD 6 Occipital Ctx	34.2	9.7
Control (Path) 3 Hippo	11.1	7.0	Control 1 Occipital Ctx	8.4	0.0
AD 1 Temporal Ctx	36.3	31.9	Control 2 Occipital Ctx	26.1	24.7
AD 2 Temporal Ctx	57.4	38.4	Control 3 Occipital Ctx	21.2	35.4
AD 3 Temporal Ctx	10.8	9.2	Control 4 Occipital Ctx	2.7	12.9
AD 4 Temporal Ctx	24.8	26.8	Control (Path) 1 Occipital Ctx	73.7	77.4
AD 5 Inf Temporal Ctx	**100.0**	76.3	Control (Path) 2 Occipital Ctx	26.1	17.8
AD 5 SupTemporal Ctx	62.0	54.3	Control (Path) 3 Occipital Ctx	5.4	3.2
AD 6 Inf Temporal Ctx	33.9	57.0	Control (Path) 4 Occipital Ctx	35.1	7.6
AD 6 Sup Temporal Ctx	47.3	69.7	Control 1 Parietal Ctx	8.7	9.9
Control 1 Temporal Ctx	15.8	8.5	Control 2 Parietal Ctx	42.9	66.0
Control 2 Temporal Ctx	12.7	25.2	Control 3 Parietal Ctx	49.0	16.3
Control 3 Temporal Ctx	49.7	36.9	Control (Path) 1 Parietal Ctx	51.8	59.9

Control 4 Temporal Ctx	17.3	16.2	Control (Path) 2 Parietal Ctx	55.5	37.1
Control (Path) 1 Temporal Ctx	87.1	74.2	Control (Path) 3 Parietal Ctx	2.6	8.8
Control (Path) 2 Temporal Ctx	83.5	**100.0**	Control (Path) 4 Parietal Ctx	69.3	56.6

Table BDE. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1706, Run 165532719	Rel. Exp.(%) Ag1851, Run 165974829	Tissue Name	Rel. Exp.(%) Ag1706, Run 165532719	Rel. Exp.(%) Ag1851, Run 165974829
Liver adenocarcinoma	0.0	0.0	Kidney (fetal)	14.3	0.0
Pancreas	0.0	0.0	Renal ca. 786-0	14.1	11.2
Pancreatic ca. CAPAN 2	0.0	6.8	Renal ca. A498	33.9	17.0
Adrenal gland	0.0	0.0	Renal ca. RXF 393	0.0	0.0
Thyroid	12.5	7.2	Renal ca. ACHN	7.0	8.8
Salivary gland	25.2	0.0	Renal ca. UO-31	0.0	15.0
Pituitary gland	46.0	63.7	Renal ca. TK-10	0.0	0.0
Brain (fetal)	25.5	22.2	Liver	15.5	8.3
Brain (whole)	**100.0**	43.2	Liver (fetal)	6.7	0.0
Brain (amygdala)	40.1	34.4	Liver ca. (hepatoblast) HepG2	0.0	7.5
Brain (cerebellum)	0.0	31.9	Lung	0.0	0.0
Brain (hippocampus)	28.5	**100.0**	Lung (fetal)	6.7	33.7
Brain (substantia nigra)	21.8	0.0	Lung ca. (small cell) LX-1	0.0	0.0
Brain (thalamus)	20.9	5.6	Lung ca. (small cell) NCI-H69	0.0	0.0
Cerebral Cortex	6.5	13.8	Lung ca. (s.cell var.)	13.2	7.9

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			SHP-77		
Spinal cord	21.5	30.1	Lung ca. (large cell)NCI-H460	0.0	0.0
glio/astro U87-MG	18.0	7.7	Lung ca. (non-sm. cell) A549	0.0	0.0
glio/astro U-118-MG	6.9	0.0	Lung ca. (non-s.cell) NCI-H23	9.5	0.0
astrocytoma SW1783	20.6	7.2	Lung ca. (non-s.cell) HOP-62	7.4	0.0
neuro*; met SK-N-AS	0.0	0.0	Lung ca. (non-s.cl) NCI-H522	9.9	0.0
astrocytoma SF-539	17.1	8.8	Lung ca. (squam.) SW 900	0.0	6.1
astrocytoma SNB-75	0.0	0.0	Lung ca. (squam.) NCI-H596	8.0	0.0
glioma SNB-19	9.3	0.0	Mammary gland	0.0	0.0
glioma U251	12.8	4.5	Breast ca.* (pl.ef) MCF-7	0.0	0.0
glioma SF-295	5.2	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0	8.1
Heart (fetal)	0.0	0.0	Breast ca.* (pl.ef) T47D	6.3	0.0
Heart	0.0	15.7	Breast ca. BT-549	17.8	0.0
Skeletal muscle (fetal)	0.0	0.0	Breast ca. MDA-N	0.0	0.0
Skeletal muscle	6.3	15.4	Ovary	0.0	0.0
Bone marrow	37.6	0.0	Ovarian ca. OVCAR-3	25.9	31.6
Thymus	0.0	28.7	Ovarian ca. OVCAR-4	11.3	19.1
Spleen	1.7	0.0	Ovarian ca. OVCAR-5	6.3	11.3
Lymph node	21.2	33.0	Ovarian ca. OVCAR-8	0.0	0.0
Colorectal	11.1	0.0	Ovarian ca. IGROV-1	0.0	0.0

Stomach	9.4	8.9	Ovarian ca.* (ascites) SK-OV-3	0.0	10.7
Small intestine	0.0	0.0	Uterus	0.0	15.0
Colon ca. SW480	7.1	0.0	Plancenta	0.0	9.9
Colon ca.* SW620(SW480 met)	13.1	0.0	Prostate	6.3	0.0
Colon ca. HT29	0.0	0.0	Prostate ca.* (bone met)PC-3	9.4	15.4
Colon ca. HCT-116	6.7	0.0	Testis	25.3	23.5
Colon ca. CaCo-2	18.0	5.5	Melanoma Hs688(A).T	0.0	8.1
Colon ca. tissue(ODO3866)	0.0	0.0	Melanoma* (met) Hs688(B).T	0.0	7.9
Colon ca. HCC-2998	0.0	0.0	Melanoma UACC-62	0.0	2.5
Gastric ca.* (liver met) NCI-N87	48.6	9.3	Melanoma M14	0.0	0.0
Bladder	9.0	18.2	Melanoma LOX IMVI	0.0	0.0
Trachea	0.0	7.9	Melanoma* (met) SK-MEL-5	8.3	0.0
Kidney	0.0	38.4	Adipose	13.9	15.5

Table BDF. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag1706, Run 173750214	Rel. Exp.(%) Ag1851, Run 174148763	Tissue Name	Rel. Exp.(%) Ag1706, Run 173750214	Rel. Exp.(%) Ag1851, Run 174148763
Normal Colon	4.7	10.0	Kidney Margin (OD04348)	19.3	69.3
Colon cancer (OD06064)	0.0	8.2	Kidney malignant cancer (OD06204B)	4.8	0.0
Colon Margin (OD06064)	2.5	0.0	Kidney normal adjacent tissue (OD06204E)	0.0	0.0
Colon cancer (OD06159)	0.0	0.0	Kidney Cancer (OD04450-01)	49.7	35.4

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Colon Margin (OD06159)	11.6	0.0	Kidney Margin (OD04450-03)	12.5	48.0
Colon cancer (OD06297-04)	0.0	0.0	Kidney Cancer 8120613	0.0	0.0
Colon Margin (OD06297-015)	0.0	0.0	Kidney Margin 8120614	0.0	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	0.0	Kidney Cancer 9010320	0.0	0.0
CC Margin (ODO3921)	4.0	8.8	Kidney Margin 9010321	0.0	0.0
Colon cancer metastasis (OD06104)	0.0	0.0	Kidney Cancer 8120607	0.0	0.0
Lung Margin (OD06104)	0.0	0.0	Kidney Margin 8120608	0.0	9.9
Colon mets to lung (OD04451-01)	0.0	0.0	Normal Uterus	11.0	33.4
Lung Margin (OD04451-02)	11.4	11.1	Uterine Cancer 064011	0.0	7.2
Normal Prostate	19.1	9.9	Normal Thyroid	15.1	0.0
Prostate Cancer (OD04410)	0.0	0.0	Thyroid Cancer 064010	9.5	0.0
Prostate Margin (OD04410)	0.0	0.0	Thyroid Cancer A302152	11.6	27.5
Normal Ovary	0.0	0.0	Thyroid Margin A302153	5.3	24.7
Ovarian cancer (OD06283-03)	4.8	0.0	Normal Breast	30.6	36.1
Ovarian Margin (OD06283-07)	2.8	22.1	Breast Cancer (OD04566)	0.0	0.0
Ovarian Cancer 064008	79.6	9.9	Breast Cancer 1024	4.9	0.0
Ovarian cancer (OD06145)	6.8	10.4	Breast Cancer (OD04590-01)	0.0	9.2
Ovarian Margin (OD06145)	0.0	15.5	Breast Cancer Mets (OD04590-03)	42.0	26.2
Ovarian cancer (OD06455-03)	5.8	25.3	Breast Cancer Metastasis (OD04655-05)	17.3	42.0
Ovarian Margin (OD06455-07)	11.8	11.7	Breast Cancer 064006	0.0	0.0

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Normal Lung	4.8	11.0	Breast Cancer 9100266	0.0	0.0
Invasive poor diff. lung adeno (ODO4945-01	25.0	12.1	Breast Margin 9100265	12.8	0.0
Lung Margin (ODO4945-03)	10.7	26.2	Breast Cancer A209073	11.8	7.5
Lung Malignant Cancer (OD03126)	0.0	7.7	Breast Margin A2090734	10.2	28.1
Lung Margin (OD03126)	0.0	0.0	Breast cancer (OD06083)	21.3	31.0
Lung Cancer (OD05014A)	5.5	0.0	Breast cancer node metastasis (OD06083)	35.8	31.9
Lung Margin (OD05014B)	11.9	8.2	Normal Liver	**100.0**	**100.0**
Lung cancer (OD06081)	19.5	0.0	Liver Cancer 1026	0.0	0.0
Lung Margin (OD06081)	5.3	0.0	Liver Cancer 1025	37.6	24.7
Lung Cancer (OD04237-01)	5.8	0.0	Liver Cancer 6004-T	5.3	11.3
Lung Margin (OD04237-02)	0.0	0.0	Liver Tissue 6004-N	6.4	0.0
Ocular Melanoma Metastasis	0.0	9.5	Liver Cancer 6005-T	0.0	5.1
Ocular Melanoma Margin (Liver)	0.0	8.1	Liver Tissue 6005-N	0.0	21.3
Melanoma Metastasis	0.0	0.0	Liver Cancer 064003	14.3	3.9
Melanoma Margin (Lung)	5.5	0.0	Normal Bladder	0.0	0.0
Normal Kidney	0.0	23.8	Bladder Cancer 1023	5.6	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	28.1	57.0	Bladder Cancer A302173	0.0	0.0
Kidney Margin (OD04338)	39.5	15.1	Normal Stomach	11.3	12.9
Kidney Ca Nuclear grade 1/2 (OD04339)	71.2	78.5	Gastric Cancer 9060397	0.0	0.0

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Kidney Margin (OD04339)	0.0	20.9	Stomach Margin 9060396	9.2	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	0.0	Gastric Cancer 9060395	48.0	0.0
Kidney Margin (OD04340)	22.4	36.3	Stomach Margin 9060394	7.6	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	5.7	0.0	Gastric Cancer 064005	0.0	0.0

Table BDG. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1706, Run 164729527	Rel. Exp.(%) Ag1851, Run 165831440	Rel. Exp.(%) Ag2544, Run 164392487	Tissue Name	Rel. Exp.(%) Ag1706, Run 164729527	Rel. Exp.(%) Ag1851, Run 165831440	Rel. Exp.(%) Ag2544, Run 164392487
Secondary Th1 act	0.0	0.0	0.0	HUVEC IL-1beta	0.0	0.0	0.0
Secondary Th2 act	0.8	2.6	5.2	HUVEC IFN gamma	5.4	5.5	9.4
Secondary Tr1 act	0.0	7.9	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0	3.1
Secondary Th1 rest	4.9	5.0	0.0	HUVEC TNF alpha + IL4	2.8	0.8	0.0
Secondary Th2 rest	0.0	5.5	0.0	HUVEC IL-11	4.5	1.5	0.0
Secondary Tr1 rest	4.2	4.4	7.1	Lung Microvascular EC none	1.4	2.8	14.4
Primary Th1 act	3.3	1.2	0.0	Lung Microvascular EC TNFalpha + IL-1beta	2.8	4.4	9.0
Primary Th2 act	1.1	4.0	0.0	Microvascular Dermal EC none	1.1	1.6	13.5
Primary Tr1 act	4.3	0.8	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	2.6	0.0
Primary Th1 rest	13.4	22.1	36.9	Bronchial epithelium	9.3	5.5	7.7

				TNFalpha + IL1beta			
Primary Th2 rest	15.5	13.6	41.2	Small airway epithelium none	3.4	2.1	0.0
Primary Tr1 rest	6.6	12.1	10.4	Small airway epithelium TNFalpha + IL-1beta	10.0	24.8	60.7
CD45RA CD4 lymphocyte act	0.7	0.4	8.7	Coronery artery SMC rest	1.3	1.6	3.4
CD45RO CD4 lymphocyte act	13.2	4.9	2.8	Coronery artery SMC TNFalpha + IL-1beta	3.5	2.2	0.0
CD8 lymphocyte act	10.3	8.2	13.4	Astrocytes rest	0.0	9.5	0.0
Secondary CD8 lymphocyte rest	1.9	7.1	16.7	Astrocytes TNFalpha + IL-1beta	2.8	19.9	13.0
Secondary CD8 lymphocyte act	3.5	6.7	0.0	KU-812 (Basophil) rest	5.4	11.8	17.0
CD4 lymphocyte none	6.0	4.3	13.1	KU-812 (Basophil) PMA/ionomycin	18.4	23.8	36.6
2ry Th1/Th2/Tr1_anti-CD95 CH11	5.6	18.7	13.0	CCD1106 (Keratinocytes) none	10.4	26.1	46.7
LAK cells rest	7.9	7.1	14.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	9.7	**100.0**	10.7
LAK cells IL-2	0.0	15.5	4.2	Liver cirrhosis	6.1	18.4	10.0
LAK cells IL-2+IL-12	8.0	15.9	11.3	Lupus kidney	2.7	27.9	13.6
LAK cells IL-2+IFN gamma	21.2	20.7	77.9	NCI-H292 none	11.6	5.1	20.0
LAK cells IL-2+IL-18	66.9	22.5	25.9	NCI-H292 IL-4	8.8	14.0	27.4
LAK cells PMA/ionomycin	1.4	0.0	0.0	NCI-H292 IL-9	4.5	6.9	39.8
NK Cells IL-2 rest	9.7	7.1	11.7	NCI-H292 IL-13	0.0	6.9	0.0
Two Way MLR 3 day	10.4	20.2	40.3	NCI-H292 IFN gamma	2.8	5.0	7.8
Two Way MLR 5 day	3.8	7.0	0.0	HPAEC none	5.7	3.2	4.0

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Two Way MLR 7 day	0.0	0.8	3.7	HPAEC TNF alpha + IL-1 beta	0.0	2.6	0.0
PBMC rest	0.1	2.5	2.9	Lung fibroblast none	4.5	6.1	0.0
PBMC PWM	20.6	6.0	19.2	Lung fibroblast TNF alpha + IL-1 beta	0.0	3.9	0.0
PBMC PHA-L	11.6	1.5	4.1	Lung fibroblast IL-4	0.0	2.9	0.0
Ramos (B cell) none	10.4	25.9	61.6	Lung fibroblast IL-9	1.3	3.3	8.1
Ramos (B cell) ionomycin	**100.0**	28.9	**100.0**	Lung fibroblast IL-13	6.5	0.0	0.0
B lymphocytes PWM	14.1	4.1	13.5	Lung fibroblast IFN gamma	5.0	3.1	15.9
B lymphocytes CD40L and IL-4	31.0	6.0	18.6	Dermal fibroblast CCD1070 rest	27.9	3.6	14.0
EOL-1 dbcAMP	2.0	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	17.0	9.6	11.2
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	1.4	0.0	6.3
Dendritic cells none	4.2	3.9	24.7	Dermal fibroblast IFN gamma	6.8	1.6	9.4
Dendritic cells LPS	1.2	3.7	17.6	Dermal fibroblast IL-4	3.9	5.1	14.5
Dendritic cells anti-CD40	2.9	1.4	3.1	IBD Colitis 2	1.7	11.7	3.1
Monocytes rest	0.7	4.9	0.0	IBD Crohn's	0.0	3.1	0.0
Monocytes LPS	2.6	15.9	16.0	Colon	9.1	8.0	10.0
Macrophages rest	6.6	11.0	21.9	Lung	1.4	3.2	8.7
Macrophages LPS	1.4	2.1	0.0	Thymus	31.4	30.6	50.0
HUVEC none	1.6	2.3	0.0	Kidney	10.4	40.9	55.1
HUVEC starved	2.2	4.6	21.6				

CNS_neurodegeneration_v1.0 Summary: <u>Ag1851/Ag2544</u> Results from two experiments with different probe and primer sets both show significant expression of the GMAC009594_C gene in the brain. While no specific association with Alzheimer's disease is

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evident from the results of these experiments, the expression of this GPCR homolog in the brain is confirmed. Please see Panel 1.3D for discussion of potential utility in the central nervous system.

Panel 1.3D Summary: Ag1706/Ag1851 Results from two experiments using different probe and primer sets show significant expression of this novel G-protein coupled receptor (GPCR) in the brain, including amygdala and hippocampus. The GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and α2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the α-adrenergic receptors have been implicated in memory. Therefore this gene may be of use as a small molecule target for the treatment of any of the described diseases. Ag2544 Expression of this gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant

activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine
5   A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional
10   experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered
15   its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

20   2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which,
25   respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback
30   inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response. The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT

neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the

5   NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig

10   Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the

15   strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis.

20   NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

25   4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9 Related Articles, Books, LinkOut

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261,

30   we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly

reduced cortical infarct volume as measured 24 h later (30% vs controls, p < 0.05). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, p < 0.05). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 2.2 Summary: Ag1706/Ag1851 Results from two experiments using the identical probe/primer set are in reasonable agreement. Expression of the GMAC009594_C gene is highest in a normal liver sample. Lower levels of expression are also seen in several kidney and breast samples, both from tumor and normal adjacent tissue. Therefore, expression of this gene may be used to distinguish liver, kidney and breast from the other samples on this panel.

Panel 4D Summary: Ag1706/1851/2544 The expression pattern of the GMAC009594_C gene with all three primer sets was similar except that the level of expression was generally higher with primer set Ag1706 than with Ag1851. Expression of the transcript is seen in LAK cells, Ramos B cells, thymus and kidney. Expression was not consistently dependent upon activation in the cell types tested. The expression of the transcript may be dependent upon the proliferation status of cells, that is, it is expressed in specific types of proliferating cells that include LAK cells, B cells and cells in the thymus and kidney. The transcript or the protein it encodes may be important for the detection LAK cells, B cells, thymus and kidney tissue. Expression of this gene in kidney was also observed in Panel 2.2.

BE. GMAC009545_A: GPCR

Expression of gene GMAC009545_A was assessed using the primer-probe set Ag1705, described in Table BEA. Results of the RTQ-PCR runs are shown in Tables BEB.

Table BEA. Probe Name Ag1705

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ccgtctattctactgcatttgc-3'	22	211	480
Probe	TET-5'-cccaaaatgattgttgacttgctctctg-3'-TAMRA	28	234	481
Reverse	5'-atacaaccctgaaaggaaatgg-3'	22	271	482

Table BEB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1705, Run 165763028	Tissue Name	Rel. Exp.(%) Ag1705, Run 165763028
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0

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LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	52.5
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	4.9
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1705 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag1705 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1705 Significant expression of the GMAC009545_A gene is detected in a liver cirrhosis sample (CT = 34.1). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

BF. GMAC005962_B: GPCR

Expression of gene GMAC005962_B was assessed using the primer-probe set Ag1582, described in Table BFA. Results of the RTQ-PCR runs are shown in Table BFB.

Table BFA. Probe Name Ag1582

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atgatcttcgttccaagcattt-3'	22	778	483
Probe	TET-5'-acctctatgcccggcccttcact-3'-TAMRA	23	800	484
Reverse	5'-gatggacacaagcttgtccat-3'	21	832	485

Table BFB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1582, Run 165820889	Tissue Name	Rel. Exp.(%) Ag1582, Run 165820889
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	3.7	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0

Primary Th1 rest	8.2	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	4.1	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	7.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	3.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	4.3	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L	0.0	Dermal fibroblast	0.0

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and IL-4		CCD1070 rest	
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	2.4
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	2.6	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	12.5
Macrophages LPS	0.0	Thymus	4.2
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1582 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag1582 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1582 Significant expression of the GMAC005962_B gene is detected in a liver cirrhosis sample (CT = 34.4). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

BG. GMAL163152_C: GPCR

Expression of gene GMAL163152_C was assessed using the primer-probe sets Ag1580, Ag1581 and Ag1727, described in Tables BGA, BGB and BGC. Results of the RTQ-PCR runs are shown in Tables BGD and BGE.

Table BGA. Probe Name Ag1580

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Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ccaatgtggtagacagcattt-3'	22	515	486
Probe	TET-5'-cctccctttggttactaagcttgcctg-3'-TAMRA	27	543	487
Reverse	5'-ctgttggcaacaatgactacct-3'	22	590	488

Table BGB. Probe Name Ag1581

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-aattcattttgctgggactga-3'	21	35	489
Probe	TET-5'-ttcttctctttgccctcttctcggtt-3'-TAMRA	26	77	490
Reverse	5'-acccaaaactgtgaccacatag-3'	22	105	491

Table BGC. Probe Name Ag1727

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-aattcattttgctgggactga-3'	21	35	492
Probe	TET-5'-ttcttctctttgccctcttctcggtt-3'-TAMRA	26	77	493
Reverse	5'-acccaaaactgtgaccacatag-3'	22	105	494

Table BGD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1580, Run 165920261	Tissue Name	Rel. Exp.(%) Ag1580, Run 165920261
Liver adenocarcinoma	51.1	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	18.7
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	19.5	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0

Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	10.2	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	12.8
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0

Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table BGE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1580, Run 165820874	Rel. Exp.(%) Ag1727, Run 165767201	Tissue Name	Rel. Exp.(%) Ag1580, Run 165820874	Rel. Exp.(%) Ag1727, Run 165767201
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	0.0	0.0
Secondary Tr1 act	0.0	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	7.2	Microsvasular Dermal EC TNFalpha + IL-	0.0	0.0

			1beta		
Primary Th1 rest	0.0	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	0.0	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0	0.0
CD45RA CD4 lymphocyte act	0.0	0.0	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8 lymphocyte rest	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0
Secondary CD8 lymphocyte act	2.9	0.0	KU-812 (Basophil) rest	0.0	0.0
CD4 lymphocyte none	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	0.0	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	0.0	0.0	Liver cirrhosis	**100.0**	**100.0**
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	0.0	0.0
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+IL-18	0.0	0.0	NCI-H292 IL-4	0.0	0.0
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	0.0	0.0
NK Cells IL-2 rest	0.0	0.0	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	0.0	NCI-H292 IFN gamma	0.0	0.0

Two Way MLR 5 day	0.0	0.0	HPAEC none	0.0	0.0
Two Way MLR 7 day	0.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	0.7
PBMC rest	0.0	0.0	Lung fibroblast none	0.0	0.0
PBMC PWM	0.0	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	0.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	1.1
B lymphocytes CD40L and IL-4	0.0	5.7	Dermal fibroblast CCD1070 rest	0.0	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0
Dendritic cells none	0.0	0.0	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	0.0	1.0	Dermal fibroblast IL-4	0.0	0.0
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	3.9	16.2
Monocytes rest	0.0	0.0	IBD Crohn's	0.0	0.0
Monocytes LPS	0.0	0.0	Colon	6.8	8.8
Macrophages rest	0.0	0.0	Lung	6.9	0.0
Macrophages LPS	0.0	0.0	Thymus	0.0	0.0
HUVEC none	0.0	0.0	Kidney	0.0	0.0
HUVEC starved	0.0	0.0			

Panel 1.3D Summary: <u>Ag1580</u> Expression of the GMAL163152_C gene is restricted to the spleen (CT = 34.4), an important site of secondary immune responses. Therefore, expression of this gene can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR

may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases.

Panel 2.2 Summary: Ag1580 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5   **Panel 4D Summary:** Ag1580/Ag1727 The GMAL163152_C transcript is only detected in liver cirrhosis. Furthermore, this transcript is not detected in normal liver in Panel 1.3D, suggesting that GMAL163152_C gene expression is unique to liver cirrhosis. The GMAL163152_C gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition,
10   antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

BH. GMAL359218_E: GPCR

Expression of gene GMAL359218_E was assessed using the primer-probe set Ag1579, described in Table BHA. Results of the RTQ-PCR runs are shown in Tables BHB
15   and BHC.

Table BHA. Probe Name Ag1579

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cagtaacgacccctaagcttct-3'	22	232	495
Probe	TET-5'-tcatttcctatgaccaatgcattgtg-3'-TAMRA	26	280	496
Reverse	5'-caaaatgcaggaagaagagttg-3'	22	306	497

Table BHB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1579, Run 165920250	Tissue Name	Rel. Exp.(%) Ag1579, Run 165920250
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	1.3
Thyroid	0.0	Renal ca. ACHN	0.0

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Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.7
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
Neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
Glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	6.7	Ovarian ca.	0.0

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		OVCAR-5	
Lymph node	**100.0**	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	1.7
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.7
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table BHC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1579, Run 165820830	Tissue Name	Rel. Exp.(%) Ag1579, Run 165820830
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0

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Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell)	0.0	Lung fibroblast IL-13	0.0

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ionomycin			
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	4.1	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	18.7
Monocytes rest	0.0	IBD Crohn's	5.0
Monocytes LPS	0.0	Colon	4.5
Macrophages rest	0.0	Lung	6.9
Macrophages LPS	0.0	Thymus	3.8
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1579 The GMAL359218_E gene is expressed in the lymph node (CT = 31) and to a lesser extent in spleen (CT = 34.9). Therefore, expression of this gene can be used to distinguish lymph node and spleen from the other samples on this panel. The transcript is also expressed in cirrhotic liver in Panel 4D. Lymph nodes and spleen have many similarities: both contain T cells, B cells and other cell types that regulate the function and survival of lymphocytes. In chronically inflamed tissues such as cirrhotic liver, lymph node-like structures that can include high endothelial venules and germinal centers may be present. The transcript encodes a putative GPCR that may play an important role in regulating cellular activation or migration through the lymph nodes, spleen or inflamed tissue. Therefore, therapies designed with the protein encoded for by this transcript could be important in the regulation of lymphocyte function.

Panel 2.2 Summary: Ag1579 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1579 Significant expression of this gene is detected in a liver cirrhosis sample (CT = 33.6). Furthermore, expression of this gene is not detected in normal

liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

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BI. GMAL163152_B: GPCR

Expression of gene GMAL163152_B was assessed using the primer-probe set Ag1578, described in Table BIA. Results of the RTQ-PCR runs are shown in Table BIB.

Table BIA. Probe Name Ag1578

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tctgataatcatggcctttgac-3'	22	329	498
Probe	TET-5'-tgtagccatatgtaaacccctgcact-3'-TAMRA	26	356	499
Reverse	5'-ttgtggctcatgattgtcctat-3'	22	382	500

10   Table BIB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1578, Run 165322928	Tissue Name	Rel. Exp.(%) Ag1578, Run 165322928
Secondary Th1 act	0.0	HUVEC IL-1beta	8.8
Secondary Th2 act	11.3	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium	0.0

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		none	
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0

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EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1578 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag1578 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1578 Significant expression of the GMAL163152_B gene is detected in a liver cirrhosis sample (CT = 33.8). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

BJ. GMAL359218_D: GPCR

Expression of gene GMAL359218_D was assessed using the primer-probe sets Ag1575, Ag2464 and Ag2465, described in Tables BJA, BJB and BJC. Results of the RTQ-PCR runs are shown in Table BJD.

Table BJA. Probe Name Ag1575

Primers	Sequences	Length	Start Position	SEQ ID NO:

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Forward	5'-aacctagctttcctggacatgt-3'	22	212	501
Probe	TET-5'-tcatttgccactcccaagatgatcag-3'-TAMRA	26	242	502
Reverse	5'-acatcctccaaaggagatgagt-3'	22	289	503

Table BJB. Probe Name Ag2464

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cagaatttgtgttgcatgga-3'	20	45	504
Probe	TET-5'-ctctgcacttcacgacatcttcaaaa-3'-TAMRA	26	65	505
Reverse	5'-ccagcataatggccacatag-3'	20	118	506

Table BJC. Probe Name Ag2465

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cagaatttgtgttgcatgga-3'	20	45	507
Probe	TET-5'-ctctgcacttcacgacatcttcaaaa-3'-TAMRA	26	65	508
Reverse	5'-ccagcataatggccacatag-3'	20	118	509

Table BJD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1575, Run 165725924	Tissue Name	Rel. Exp.(%) Ag1575, Run 165725924
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium	0.0

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		none	
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.9	Liver cirrhosis	25.2
LAK cells IL-2+IL-12	**100.0**	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	2.2
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.6
PBMC rest	0.5	Lung fibroblast none	1.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0

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EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	1.6
Monocytes rest	1.1	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.8
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	2.9	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag1575/Ag2464/Ag2465 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag1575/Ag2464/Ag2465 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5   **Panel 2.2 Summary:** Ag1575 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1575 Expression of the GMAL359218_D gene is highest in lymphokine-activated killer (LAK cells) treated with IL-2 and IL-12 (CT = 31.8). Since these cells are involved in tumor immunology and tumor cell clearance, as well as virally and

10 bacterial infected cells. Therefore, modulation of the activity of this gene or its protein product with a small molecule drug or antibody may alter the functions of these cells and lead to improvement of symptoms associated with these conditions. In addition, low expression is also detected in a liver cirrhosis sample. Furthermore, no expression in normal liver is seen in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a

15 putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis. Ag2464/Ag2465 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

BK. GMAL359218_A: GPCR

Expression of gene GMAL359218_A was assessed using the primer-probe sets Ag1572 and Ag1578, described in Tables BKA and BKB. Results of the RTQ-PCR runs are shown in Table BKC.

Table BKA. Probe Name Ag1572

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ttggcaagcaataaaactcttg-3'	22	796	510
Probe	TET-5'-cagttatcacacccttactgaatccga-3'-TAMRA	27	830	511
Reverse	5'-ggcctcttgcattttcttattt-3'	22	873	512

Table BKB. Probe Name Ag1578

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tctgataatcatggcctttgac-3'	22	345	513
Probe	TET-5'-tgtagccatatgtaaacccctgcact-3'-TAMRA	26	372	514
Reverse	5'-ttgtggctcatgattgtcctat-3'	22	398	515

Table BKC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1578, Run 165322928	Tissue Name	Rel. Exp.(%) Ag1578, Run 165322928
Secondary Th1 act	0.0	HUVEC IL-1beta	8.8
Secondary Th2 act	11.3	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0

Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L	0.0	Dermal fibroblast	0.0

and IL-4		CCD1070 rest	
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1572/Ag1578 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag1572/Ag1578 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5   **Panel 4D Summary:** Ag1578 Significant expression of this gene is detected in a liver cirrhosis sample (CT = 33.8). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR

10   could also be used for the diagnosis of liver cirrhosis. Ag1572 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

BL. GMAC006313_A: GPCR

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Expression of gene GMAC006313_A was assessed using the primer-probe sets Ag1567 and Ag1915, described in Tables BLA and BLB. Results of the RTQ-PCR runs are shown in Table BLC.

Table BLA. Probe Name Ag1567

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cagtgacaccagtctcaatgaa-3'	22	580	516
Probe	TET-5'-cttcatccagacagccacggtgttag-3'-TAMRA	26	625	517
Reverse	5'-gaagccataagacaccgtgata-3'	22	652	518

5   Table BLB. Probe Name Ag1915

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cagtgacaccagtctcaatgaa-3'	22	580	519
Probe	TET-5'-cttcatccagacagccacggtgttag-3'-TAMRA	26	625	520
Reverse	5'-gaagccataagacaccgtgata-3'	22	652	521

Table BLC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1567, Run 165301511	Rel. Exp.(%) Ag1915, Run 160653158	Tissue Name	Rel. Exp.(%) Ag1567, Run 165301511	Rel. Exp.(%) Ag1915, Run 160653158
Secondary Th1 act	18.2	29.3	HUVEC IL-1beta	7.7	9.7
Secondary Th2 act	3.6	14.8	HUVEC IFN gamma	72.2	94.6
Secondary Tr1 act	24.0	24.5	HUVEC TNF alpha + IFN gamma	24.7	14.7
Secondary Th1 rest	29.1	21.2	HUVEC TNF alpha + IL4	0.0	15.6
Secondary Th2 rest	20.6	14.6	HUVEC IL-11	34.4	47.0
Secondary Tr1 rest	37.4	23.3	Lung Microvascular EC none	49.7	61.6
Primary Th1 act	26.8	4.7	Lung Microvascular EC TNFalpha + IL-1beta	58.2	33.0

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Primary Th2 act	5.3	18.4	Microvascular Dermal EC none	91.4	57.0
Primary Tr1 act	29.7	25.2	Microsvasular Dermal EC TNFalpha + IL-1beta	13.7	34.9
Primary Th1 rest	93.3	58.2	Bronchial epithelium TNFalpha + IL1beta	32.3	5.2
Primary Th2 rest	33.7	39.0	Small airway epithelium none	8.0	15.3
Primary Tr1 rest	26.8	5.2	Small airway epithelium TNFalpha + IL-1beta	39.5	39.2
CD45RA CD4 lymphocyte act	5.8	15.7	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	22.1	3.7	Coronery artery SMC TNFalpha + IL-1beta	9.1	0.0
CD8 lymphocyte act	13.7	10.7	Astrocytes rest	0.0	10.4
Secondary CD8 lymphocyte rest	25.7	14.1	Astrocytes TNFalpha + IL-1beta	0.0	0.0
Secondary CD8 lymphocyte act	7.6	5.6	KU-812 (Basophil) rest	16.3	13.8
CD4 lymphocyte none	8.1	5.1	KU-812 (Basophil) PMA/ionomycin	25.7	46.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	**100.0**	46.7	CCD1106 (Keratinocytes) none	11.8	0.0
LAK cells rest	14.6	15.4	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	0.0
LAK cells IL-2	19.2	6.7	Liver cirrhosis	17.0	22.8
LAK cells IL-2+IL-12	28.7	44.1	Lupus kidney	15.4	0.0
LAK cells IL-2+IFN gamma	32.5	55.5	NCI-H292 none	18.8	17.0
LAK cells IL-2+ IL-18	24.1	12.9	NCI-H292 IL-4	14.6	15.2

LAK cells PMA/ionomycin	0.0	8.5	NCI-H292 IL-9	6.6	16.4
NK Cells IL-2 rest	4.0	11.5	NCI-H292 IL-13	0.0	8.8
Two Way MLR 3 day	33.0	11.1	NCI-H292 IFN gamma	19.3	4.4
Two Way MLR 5 day	11.5	6.8	HPAEC none	37.9	59.0
Two Way MLR 7 day	9.8	13.9	HPAEC TNF alpha + IL-1 beta	16.4	62.4
PBMC rest	5.2	0.0	Lung fibroblast none	13.9	20.7
PBMC PWM	42.3	23.3	Lung fibroblast TNF alpha + IL-1 beta	6.4	0.0
PBMC PHA-L	0.0	7.6	Lung fibroblast IL-4	28.3	22.4
Ramos (B cell) none	28.5	24.1	Lung fibroblast IL-9	23.3	0.0
Ramos (B cell) ionomycin	0.0	14.3	Lung fibroblast IL-13	23.3	6.3
B lymphocytes PWM	32.5	25.3	Lung fibroblast IFN gamma	4.0	21.8
B lymphocytes CD40L and IL-4	63.3	22.5	Dermal fibroblast CCD1070 rest	29.7	2.9
EOL-1 dbcAMP	17.4	15.1	Dermal fibroblast CCD1070 TNF alpha	72.7	71.7
EOL-1 dbcAMP PMA/ionomycin	21.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	5.0	0.0
Dendritic cells none	29.9	0.0	Dermal fibroblast IFN gamma	12.8	17.9
Dendritic cells LPS	20.3	0.0	Dermal fibroblast IL-4	18.7	14.4
Dendritic cells anti-CD40	15.0	25.9	IBD Colitis 2	7.1	0.0
Monocytes rest	8.4	14.3	IBD Crohn's	0.0	11.6
Monocytes LPS	11.3	0.0	Colon	36.6	6.4
Macrophages rest	24.5	22.5	Lung	38.4	20.7
Macrophages LPS	0.0	0.0	Thymus	34.4	21.5
HUVEC none	40.6	45.4	Kidney	60.3	59.9
HUVEC starved	53.6	**100.0**			

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Panel 1.3D Summary: Ag1567/Ag1915 Results from two experiments using identical probe/primer sets are very disparate and no conclusions can be drawn from the data (data not shown).

Panel 2.2 Summary: Ag1567 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1567/1915 Consistent but low expression of the GMAC006313_A gene is observed in kidney, primary Th1 and Th2 cells, primary T cells simulated with anti-CD95, as well as in HUVEC and HPAEC endothelial cells and dermal fibroblasts. Expression of this gene in dermal fibroblast cells is induced by treatment with TNFalpha. The protein encoded for by the transcript is a putative GPCR that may be important in T cell activation or polarization and dermal fibroblast response to proinflammatory cytokines. Therefore, therapies designed with the protein encoded for by this transcript could be important in diseases mediated by T cells including asthma, IBD, or arthritis. Based on the expression of this gene in dermal fibrblasts, these therapies may also be important for the treatment of skin diseases including psoriasis and allergy.

BM. CG55970-01: OLFACTORY RECEPTOR

Expression of gene CG55970-01 was assessed using the primer-probe set Ag5095, described in Table BMA. Results of the RTQ-PCR runs are shown in Tables BMB and BMC.

Table BMA. Probe Name Ag5095

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ttctgctgctgctttatgct-3'	20	94	522
Probe	TET-5'-cctgggcaacatcctcatcctctta-3'-TAMRA	26	122	523
Reverse	5'-gcaagctctgctcttcctttt-3'	20	152	524

Table BMB. General_screening_panel_v1.5

Tissue Name	Rel. Exp.(%) Ag5095, Run	Rel. Exp.(%) Ag5095, Run	Tissue Name	Rel. Exp.(%) Ag5095, Run	Rel. Exp.(%) Ag5095, Run

	228727262	229384819		228727262	229384819
Adipose	0.1	0.1	Renal ca. TK-10	0.1	0.0
Melanoma* Hs688(A).T	0.0	0.0	Bladder	0.4	0.4
Melanoma* Hs688(B).T	0.0	0.0	Gastric ca. (liver met.) NCI-N87	0.2	0.2
Melanoma* M14	0.2	0.1	Gastric ca. KATO III	0.2	0.3
Melanoma* LOXIMVI	2.0	1.5	Colon ca. SW-948	0.0	0.0
Melanoma* SK-MEL-5	23.3	24.3	Colon ca. SW480	0.2	0.2
Squamous cell carcinoma SCC-4	0.0	0.0	Colon ca.* (SW480 met) SW620	1.6	1.1
Testis Pool	0.2	0.2	Colon ca. HT29	0.0	0.0
Prostate ca.* (bone met) PC-3	0.0	0.0	Colon ca. HCT-116	**100.0**	**100.0**
Prostate Pool	0.1	0.2	Colon ca. CaCo-2	0.1	0.0
Placenta	0.0	0.1	Colon cancer tissue	0.0	0.1
Uterus Pool	0.2	0.1	Colon ca. SW1116	0.0	0.0
Ovarian ca. OVCAR-3	0.1	0.1	Colon ca. Colo-205	0.0	0.0
Ovarian ca. SK-OV-3	0.5	0.7	Colon ca. SW-48	0.0	0.0
Ovarian ca. OVCAR-4	0.0	0.0	Colon Pool	0.7	0.5
Ovarian ca. OVCAR-5	0.0	0.0	Small Intestine Pool	0.6	1.1
Ovarian ca. IGROV-1	0.0	0.0	Stomach Pool	0.3	0.3
Ovarian ca. OVCAR-8	0.0	0.0	Bone Marrow Pool	0.3	0.2
Ovary	0.2	0.3	Fetal Heart	0.3	0.3
Breast ca. MCF-7	0.0	0.0	Heart Pool	0.2	0.1
Breast ca. MDA-MB-231	0.0	0.0	Lymph Node Pool	0.5	0.6

Breast ca. BT 549	0.0	0.0	Fetal Skeletal Muscle	0.1	0.1
Breast ca. T47D	0.0	0.0	Skeletal Muscle Pool	0.1	0.0
Breast ca. MDA-N	2.2	3.0	Spleen Pool	0.1	0.1
Breast Pool	0.6	0.4	Thymus Pool	0.3	0.4
Trachea	0.1	0.2	CNS cancer (glio/astro) U87-MG	0.0	0.0
Lung	0.3	0.2	CNS cancer (glio/astro) U-118-MG	0.2	0.2
Fetal Lung	0.4	0.7	CNS cancer (neuro;met) SK-N-AS	0.0	0.0
Lung ca. NCI-N417	0.0	0.0	CNS cancer (astro) SF-539	0.0	0.0
Lung ca. LX-1	16.7	19.5	CNS cancer (astro) SNB-75	0.0	0.0
Lung ca. NCI-H146	0.1	0.0	CNS cancer (glio) SNB-19	0.0	0.0
Lung ca. SHP-77	0.3	0.1	CNS cancer (glio) SF-295	0.3	0.2
Lung ca. A549	0.1	0.0	Brain (Amygdala) Pool	0.0	0.0
Lung ca. NCI-H526	0.0	0.0	Brain (cerebellum)	0.0	0.0
Lung ca. NCI-H23	0.0	0.0	Brain (fetal)	0.1	0.1
Lung ca. NCI-H460	0.9	0.0	Brain (Hippocampus) Pool	0.0	0.0
Lung ca. HOP-62	0.0	0.0	Cerebral Cortex Pool	0.0	0.0
Lung ca. NCI-H522	0.0	0.0	Brain (Substantia nigra) Pool	0.0	0.0
Liver	0.0	0.0	Brain (Thalamus) Pool	0.1	0.1
Fetal Liver	0.0	0.1	Brain (whole)	0.1	0.1
Liver ca. HepG2	0.0	0.0	Spinal Cord Pool	0.0	0.1
Kidney Pool	0.4	0.9	Adrenal Gland	0.1	0.1
Fetal Kidney	0.7	0.5	Pituitary gland	0.0	0.1

			Pool		
Renal ca. 786-0	0.0	0.0	Salivary Gland	0.0	0.0
Renal ca. A498	0.0	0.0	Thyroid (female)	0.0	0.0
Renal ca. ACHN	0.0	0.1	Pancreatic ca. CAPAN2	0.0	0.0
Renal ca. UO-31	0.0	0.0	Pancreas Pool	0.5	0.6

Table BMC. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag5095, Run 225001774	Tissue Name	Rel. Exp.(%) Ag5095, Run 225001774
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.9
Secondary Tr1 act	0.2	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.6
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.3	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.7	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.5	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.8	Coronery artery SMC TNFalpha + IL-1beta	0.4
CD8 lymphocyte act	0.0	Astrocytes rest	0.8
Secondary CD8 lymphocyte rest	0.2	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0

CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.8
2ry Th1/Th2/Tr1_anti-CD95 CH11	1.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	1.2	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.6	NCI-H292 none	0.4
LAK cells IL-2+IFN gamma	0.0	NCI-H292 IL-4	0.0
LAK cells IL-2+ IL-18	0.2	NCI-H292 IL-9	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-13	0.0
NK Cells IL-2 rest	0.6	NCI-H292 IFN gamma	0.0
Two Way MLR 3 day	1.8	HPAEC none	0.0
Two Way MLR 5 day	1.1	HPAEC TNF alpha + IL-1 beta	0.0
Two Way MLR 7 day	0.0	Lung fibroblast none	0.0
PBMC rest	0.8	Lung fibroblast TNF alpha + IL-1 beta	0.8
PBMC PWM	0.0	Lung fibroblast IL-4	0.4
PBMC PHA-L	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) none	17.0	Lung fibroblast IL-13	1.2
Ramos (B cell) ionomycin	13.2	Lung fibroblast IFN gamma	0.4
B lymphocytes PWM	0.3	Dermal fibroblast CCD1070 rest	0.0
B lymphocytes CD40L and IL-4	0.7	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast IFN gamma	1.4
Dendritic cells none	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells LPS	0.3	Dermal Fibroblasts rest	0.0
Dendritic cells anti-CD40	0.0	Neutrophils TNFa+LPS	0.0
Monocytes rest	0.0	Neutrophils rest	2.0
Monocytes LPS	0.8	Colon	1.6
Macrophages rest	1.4	Lung	4.6
Macrophages LPS	0.0	Thymus	9.4
HUVEC none	0.2	Kidney	**100.0**

HUVEC starved	0.4		

CNS_neurodegeneration_v1.0 Summary: Ag5095 Expression of this gene is low/undetectable (CTs >35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.5 Summary: Ag5095 Expression of the CG55970-01 gene is highest in a samples derived from colon cancer cell line HCT 116 (CT = 25-26). In addition, there is relatively high expression of this gene in a lung cancer cell line (LX-1) and a melanoma cell line (SK-Mel-5). Thus, the expression of this gene could be used to distinguish samples derived from these cell lines from other samples in the panel. Moreover, therapeutic modulation of this gene, through the use of antibodies, small molecule drugs or protein therapeutics, might be of benefit in the treatment of colon cancer, lung cancer or melanoma. Among tissues with metabolic activity, this gene is expressed at low levels in pancreas and fetal heart. Therefore, the GPCR encoded by this gene may play a role in cardiovascular diseases and/or metabolic diseases, such as diabetes and obesity. Low expression is also seen in a number of other normal tissues including thymus, lymph node, bone marrow, small intestine, stomach, colon, bladder, lung, breast, and ovary (CTs = 31-35).

Panel 4.1D Summary: Ag5095 Expression of the CG55970-01 gene is highest in kidney (CT = 30). Therefore, the putative GPCR encoded for by this gene could allow cells within the kidney to respond to specific microenvironmental signals. Thus, antibody or small molecule therapies designed with the protein encoded for by this gene could modulate kidney function and be important in the treatment of inflammatory or autoimmune diseases that affect the kidney, including lupus and glomerulonephritis. In addition, this gene is expressed at low levels in Ramos B cells (CT = 33), consistent with what is observed in Panel 4D. Expression of this transcript in B cells suggests that this gene may be involved in rheumatic disease including rheumatoid arthritis, lupus, osteoarthritis, and hyperproliferative B cell disorders. In addition, expression of this gene could be used to distinguish kidney and Ramos B cells from the other samples on this panel.

BN. CG59396-01: Olfactory Receptor

Expression of gene CG59396-01 was assessed using the primer-probe set Ag1713, described in Table BNA. Results of the RTQ-PCR runs are shown in Table BNB.

Table BNA. Probe Name Ag1713

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tcattgaccatttcatctgtga-3'	22	536	525
Probe	TET-5'-ccctctgctaaaactctcctgcactga-3'-TAMRA	27	564	526
Reverse	5'-caaagagtccaaagacgtgagt-3'	22	592	527

Table BNB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1713, Run 165768303	Tissue Name	Rel. Exp.(%) Ag1713, Run 165768303
Secondary Th1 act	3.2	HUVEC IL-1beta	0.0
Secondary Th2 act	3.5	HUVEC IFN gamma	0.0
Secondary Tr1 act	4.6	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	2.1	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0

2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	7.6	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	6.5	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	2.6	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	62.0
Monocytes rest	0.0	IBD Crohn's	17.6
Monocytes LPS	0.0	Colon	2.6
Macrophages rest	0.0	Lung	7.6
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 4D Summary: <u>Ag1713</u> Highest expression of the CG59396-01 gene is seen in liver cirrhosis (CT=34.1). Furthermore, no expression in normal liver is seen in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

Low but significant expression is also seen in a sample derived from a patient with IBD colitis, but not in normal colon. This observation suggests that the protein encoded by this gene may be involved in the inflammatory bowel disease process. Therefore, therapeutic modulation of the expression or function of this gene product could potentially be useful in treating the symptoms of this disease.

BO. GMAC076959_A/CG55804-02: Olfactory Receptor

Expression of gene GMAC076959_A (also known as CG55804-02) was assessed using the primer-probe sets Ag2308, Ag1510, Ag4494 and Ag1538, described in Tables BOA, BOB, BOC and BOD. Results of the RTQ-PCR runs are shown in Tables BOE, BOF, BOG, and BOH.

<u>Table BOA</u>. Probe Name Ag2308

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-taccgatcatagcacatcatca-3'	22	347	528
Probe	TET-5'-tcagacactctgtaatagcaaacgcca-3'-TAMRA	27	314	529
Reverse	5'-tgctccttgcatacttcagact-3'	22	282	530

<u>Table BOB</u>. Probe Name Ag1510

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-attctcaagaacggaggaagat-3'	22	797	531
Probe	TET-5'-tttacagccttttcaacccgatcctg-3'-TAMRA	26	830	532
Reverse	5'-tctgcattcctaaggctgtaga-3'	22	866	533

<u>Table BOC</u>. Probe Name Ag4494

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Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-attctcaagaacggaggaagat-3'	22	797	534
Probe	TET-5'-tttacagccttttcaacccgatcctg-3'-TAMRA	26	830	535
Reverse	5'-tctgcattcctaaggctgtaga-3'	22	866	536

Table BOD. Probe Name Ag1538

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-aggaagatcctttccctgttt-3'	21	811	537
Probe	TET-5'-tacagccttttcaacccgatcctgaa-3'-TAMRA	26	832	538
Reverse	5'-ctctctttagagccccttcac-3'	22	889	539

Table BOE. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2308, Run 207970871	Tissue Name	Rel. Exp.(%) Ag2308, Run 207970871
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	0.0
AD 2 Hippo	9.8	Control (Path) 4 Temporal Ctx	10.7
AD 3 Hippo	0.0	AD 1 Occipital Ctx	24.0
AD 4 Hippo	18.2	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	16.6	AD 3 Occipital Ctx	0.0
AD 6 Hippo	81.8	AD 4 Occipital Ctx	1.2
Control 2 Hippo	0.0	AD 5 Occipital Ctx	1.8
Control 4 Hippo	38.7	AD 6 Occipital Ctx	1.9
Control (Path) 3 Hippo	1.2	Control 1 Occipital Ctx	17.6
AD 1 Temporal Ctx	16.4	Control 2 Occipital Ctx	0.0
AD 2 Temporal Ctx	14.6	Control 3 Occipital Ctx	17.2
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	30.8
AD 4 Temporal Ctx	20.4	Control (Path) 1 Occipital Ctx	0.0
AD 5 Inf Temporal Ctx	15.1	Control (Path) 2 Occipital Ctx	11.7
AD 5 Sup Temporal Ctx	27.9	Control (Path) 3 Occipital Ctx	0.0

AD 6 Inf Temporal Ctx	13.0	Control (Path) 4 Occipital Ctx	16.7
AD 6 Sup Temporal Ctx	1.6	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	0.0
Control 2 Temporal Ctx	1.2	Control 3 Parietal Ctx	0.0
Control 3 Temporal Ctx	**100.0**	Control (Path) 1 Parietal Ctx	4.0
Control 3 Temporal Ctx	38.7	Control (Path) 2 Parietal Ctx	0.0
Control (Path) 1 Temporal Ctx	16.2	Control (Path) 3 Parietal Ctx	10.3
Control (Path) 2 Temporal Ctx	0.0	Control (Path) 4 Parietal Ctx	31.0

Table BOF. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag1510, Run 222653849	Rel. Exp.(%) Ag4494, Run 222666589	Tissue Name	Rel. Exp.(%) Ag1510, Run 222653849	Rel. Exp.(%) Ag4494, Run 222666589
Adipose	14.2	6.1	Renal ca. TK-10	8.3	13.8
Melanoma* Hs688(A).T	9.0	0.0	Bladder	**100.0**	24.3
Melanoma* Hs688(B).T	4.2	6.7	Gastric ca. (liver met.) NCI-N87	3.7	9.7
Melanoma* M14	0.0	0.0	Gastric ca. KATO III	1.7	8.7
Melanoma* LOXIMVI	0.0	0.0	Colon ca. SW-948	0.0	0.0
Melanoma* SK-MEL-5	0.0	0.0	Colon ca. SW480	0.0	0.0
Squamous cell carcinoma SCC-4	0.0	0.0	Colon ca.* (SW480 met) SW620	0.0	8.2
Testis Pool	6.9	0.0	Colon ca. HT29	2.4	0.0
Prostate ca.* (bone met) PC-3	0.0	0.0	Colon ca. HCT-116	0.0	12.8
Prostate Pool	10.6	7.2	Colon ca. CaCo-2	11.0	8.4
Placenta	2.5	2.3	Colon cancer	19.3	10.3

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			tissue		
Uterus Pool	4.0	2.5	Colon ca. SW1116	0.0	0.0
Ovarian ca. OVCAR-3	12.5	8.6	Colon ca. Colo-205	0.0	0.0
Ovarian ca. SK-OV-3	2.2	3.6	Colon ca. SW-48	0.0	0.0
Ovarian ca. OVCAR-4	0.0	0.0	Colon Pool	3.0	5.5
Ovarian ca. OVCAR-5	0.0	17.2	Small Intestine Pool	11.0	6.5
Ovarian ca. IGROV-1	0.0	0.0	Stomach Pool	21.6	24.8
Ovarian ca. OVCAR-8	5.7	0.0	Bone Marrow Pool	57.4	22.4
Ovary	13.5	15.7	Fetal Heart	0.0	0.0
Breast ca. MCF-7	0.0	3.0	Heart Pool	19.1	7.3
Breast ca. MDA-MB-231	4.0	2.2	Lymph Node Pool	27.9	29.5
Breast ca. BT 549	0.0	0.0	Fetal Skeletal Muscle	0.0	0.0
Breast ca. T47D	16.2	2.2	Skeletal Muscle Pool	0.0	0.0
Breast ca. MDA-N	0.0	7.1	Spleen Pool	4.3	5.4
Breast Pool	8.3	0.0	Thymus Pool	7.9	13.1
Trachea	7.1	2.7	CNS cancer (glio/astro) U87-MG	0.0	0.0
Lung	3.4	7.2	CNS cancer (glio/astro) U-118-MG	6.7	0.0
Fetal Lung	29.9	34.9	CNS cancer (neuro;met) SK-N-AS	0.0	0.0
Lung ca. NCI-N417	0.0	0.0	CNS cancer (astro) SF-539	0.0	0.0
Lung ca. LX-1	9.2	14.7	CNS cancer (astro) SNB-75	0.0	0.0
Lung ca. NCI-H146	0.0	0.0	CNS cancer (glio) SNB-19	0.0	0.0
Lung ca.	0.0	0.0	CNS cancer	0.0	2.8

Tissue Name			Tissue Name		
SHP-77			(glio) SF-295		
Lung ca. A549	0.0	0.0	Brain (Amygdala) Pool	0.0	0.0
Lung ca. NCI-H526	0.0	0.0	Brain (cerebellum)	0.0	0.0
Lung ca. NCI-H23	3.4	4.1	Brain (fetal)	0.0	6.5
Lung ca. NCI-H460	0.0	0.0	Brain (Hippocampus) Pool	0.0	0.0
Lung ca. HOP-62	3.1	0.0	Cerebral Cortex Pool	0.0	0.0
Lung ca. NCI-H522	0.0	0.0	Brain (Substantia nigra) Pool	0.0	0.0
Liver	0.0	0.0	Brain (Thalamus) Pool	0.0	8.5
Fetal Liver	6.9	9.9	Brain (whole)	0.0	0.0
Liver ca. HepG2	8.8	14.1	Spinal Cord Pool	0.0	9.7
Kidney Pool	19.2	4.5	Adrenal Gland	3.7	3.9
Fetal Kidney	70.7	**100.0**	Pituitary gland Pool	0.0	3.5
Renal ca. 786-0	34.6	32.8	Salivary Gland	3.2	0.0
Renal ca. A498	16.2	5.9	Thyroid (female)	3.2	3.1
Renal ca. ACHN	3.4	2.8	Pancreatic ca. CAPAN2	2.4	0.0
Renal ca. UO-31	1.9	2.6	Pancreas Pool	17.9	18.3

Table BOG. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1510, Run 141938638	Tissue Name	Rel. Exp.(%) Ag1510, Run 141938638
Endothelial cells	0.0	Renal ca. 786-0	11.9
Heart (Fetal)	0.0	Renal ca. A498	24.3
Pancreas	0.6	Renal ca. RXF 393	22.2
Pancreatic ca. CAPAN 2	0.3	Renal ca. ACHN	2.6
Adrenal Gland	2.7	Renal ca. UO-31	43.8
Thyroid	1.0	Renal ca. TK-10	8.2
Salivary gland	49.7	Liver	11.2

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Pituitary gland	0.0	Liver (fetal)	3.1
Brain (fetal)	0.0	Liver ca. (hepatoblast) HepG2	55.1
Brain (whole)	0.0	Lung	0.0
Brain (amygdala)	0.0	Lung (fetal)	0.0
Brain (cerebellum)	0.0	Lung ca. (small cell) LX-1	4.6
Brain (hippocampus)	0.0	Lung ca. (small cell) NCI-H69	61.1
Brain (thalamus)	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Cerebral Cortex	0.0	Lung ca. (large cell)NCI-H460	46.7
Spinal cord	0.0	Lung ca. (non-sm. cell) A549	23.0
glio/astro U87-MG	0.0	Lung ca. (non-s.cell) NCI-H23	6.1
glio/astro U-118-MG	2.3	Lung ca. (non-s.cell) HOP-62	51.1
astrocytoma SW1783	14.7	Lung ca. (non-s.cl) NCI-H522	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (squam.) SW 900	37.9
astrocytoma SF-539	4.5	Lung ca. (squam.) NCI-H596	27.7
astrocytoma SNB-75	0.0	Mammary gland	15.4
glioma SNB-19	13.8	Breast ca.* (pl.ef) MCF-7	2.5
glioma U251	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
glioma SF-295	7.3	Breast ca.* (pl. ef) T47D	1.8
Heart	2.8	Breast ca. BT-549	6.4
Skeletal Muscle	0.0	Breast ca. MDA-N	19.9
Bone marrow	2.9	Ovary	1.7
Thymus	0.0	Ovarian ca. OVCAR-3	6.8
Spleen	0.0	Ovarian ca. OVCAR-4	11.8
Lymph node	1.3	Ovarian ca. OVCAR-5	**100.0**
Colorectal Tissue	14.0	Ovarian ca. OVCAR-8	42.3

Stomach	3.6	Ovarian ca. IGROV-1	0.0
Small intestine	0.3	Ovarian ca. (ascites) SK-OV-3	0.0
Colon ca. SW480	0.0	Uterus	0.3
Colon ca.* SW620 (SW480 met)	0.6	Placenta	3.8
Colon ca. HT29	27.0	Prostate	12.1
Colon ca. HCT-116	7.2	Prostate ca.* (bone met) PC-3	6.3
Colon ca. CaCo-2	0.0	Testis	7.1
Colon ca. Tissue (ODO3866)	30.8	Melanoma Hs688(A).T	11.9
Colon ca. HCC-2998	27.5	Melanoma* (met) Hs688(B).T	27.5
Gastric ca.* (liver met) NCI-N87	12.6	Melanoma UACC-62	0.0
Bladder	83.5	Melanoma M14	67.4
Trachea	0.0	Melanoma LOX IMVI	0.0
Kidney	**100.0**	Melanoma* (met) SK-MEL-5	0.0
Kidney (fetal)	14.2		

Table BOH. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2308, Run 158927487	Tissue Name	Rel. Exp.(%) Ag2308, Run 158927487
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	17.4
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	17.2	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	4.4
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	11.3	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0

Primary Th1 rest	24.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	14.5	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	15.1
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	6.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	29.1
LAK cells IL-2+IL-12	0.0	Lupus kidney	9.9
LAK cells IL-2+IFN gamma	21.8	NCI-H292 none	26.6
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	28.7
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	37.9
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	10.6	NCI-H292 IFN gamma	13.3
Two Way MLR 5 day	21.5	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	11.3
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	14.6	Lung fibroblast IL-4	18.6
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	15.9
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	22.2
B lymphocytes CD40L	0.0	Dermal fibroblast	0.0

and IL-4		CCD1070 rest	
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	6.7
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	27.5
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	8.7
Macrophages rest	7.5	Lung	47.0
Macrophages LPS	0.0	Thymus	**100.0**
HUVEC none	0.0	Kidney	5.8
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag2308 The GMAC076959_A gene is expressed at low levels in the brains of both normal and Alzheimer's disease patients and encodes a putative GPCR. Several neurotransmitter receptors are GPCRs, including the dopamine receptor family, the serotonin receptor family, the GABAB receptor, muscarinic acetylcholine receptors, and others; thus this GPCR may represent a novel neurotransmitter receptor. Targeting various neurotransmitter receptors (dopamine, serotonin) has proven to be an effective therapy in psychiatric illnesses such as schizophrenia, bipolar disorder, and depression. Furthermore, the cerebral cortex and hippocampus are regions of the brain that are known to be involved in Alzheimer's disease, seizure disorders, and in the normal process of memory formation. Therefore, therapeutic modulation of this gene or its protein product may be beneficial in the treatment of one or more of these diseases, as may stimulation and/or blockade of the receptor coded for by the gene. Ag1510/Ag4494 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or

5   genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.)

10   reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that

15   were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like

20   effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant

25   agents.

2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

30   Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment

desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response.

5   The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at

10   alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

15

3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many
20   neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating
25   disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA
30   receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9

5   Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly

10   reduced cortical infarct volume as measured 24 h later (30% vs controls, $p < 0.05$). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, $p < 0.05$). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

15   **General_screening_panel_v1.4 Summary:** Ag1510/Ag4494 Results from two experiments using probe/primer sets with identical sequences gave results that are in good agreement. Expression of the GMAC076959_A gene is highest in the bladder and fetal kidney (CTs=32.5-33.5). Thus, expression of this gene could be used to distinguish bladder and kidney from the other samples on this panel. In addition, this gene may play a role in the

20   normal functioning of these organs.

Panel 1.2 Summary: Ag1510 Moderate expression of the GMAC076959_A gene is detected in both adult kidney tissue and ovarian cancer cell lines (CTs = 31.4). This result suggests that expression of this gene could be used to distinguish kidney and ovarian cancer cell lines from the other samples on this panel. This gene is also expressed at low levels in a

25   wide variety of both healthy tissues and cancerous cell lines. Healthy tissues demonstrating significant expression of the GMAC076959_A gene include bladder and salivary gland tissue. This result is consistent with what is observed in General_screening_panel_v1.4. Cancerous cell lines demonstrating expression of the GMAC076959_A gene include lung, kidney, colon and other ovarian cancer cell lines. Thus, expression of this gene could

30   potentially be used to distinguish cancer cells from their normal counterparts. Furthermore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs or antibodies, may be of utility in the treatment of ovarian, lung, kidney or

colon cancer. Ag1538 Expression of this gene is low/undetectable (CTs > 35) across all of the samples in this panel (data not shown).

Panel 1.3D Summary: Ag2308 Expression of this gene is low/undetectable (CTs > 35) across all of the samples in this panel (data not shown).

Panel 4.1D Summary: Ag1510/Ag4494 Expression of this gene is low/undetectable (CTs > 35) across all of the samples in this panel (data not shown).

Panel 4D Summary: Ag2308 Expression of the GMAC076959_A gene is detected in the thymus (CT = 33.3) and lung (CT = 34.4). Thus, expression of this gene could be used as a marker to detect the presence of thymus or lung tissue. The putative GPCR encoded for by this gene may also play an important role in the normal homeostasis of these tissues. Therefore, therapeutics designed with the GMAC076959_A gene protein product could be important for maintaining or restoring normal function to these organs during inflammation. Ag1538 Expression of the GMAC076959_A gene is low/undetectable (CT values > 35) across all of the samples on this panel (data not shown).

BP. GMAC076959_C/CG92751-02: Olfactory Receptor

Expression of gene GMAC076959_C (also known as CG92751-02) was assessed using the primer-probe set Ag1511, described in Table BPA. Results of the RTQ-PCR runs are shown in Tables BPB, BPC, BPD and BPE.

Table BPA. Probe Name Ag1511

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ccacttctgtgaaatcctgtct-3'	22	523	540
Probe	TET-5'-ctcaagttggcctgtgctgacacct-3'-TAMRA	25	548	541
Reverse	5'-gcaaagatgaccacctggtt-3'	20	578	542

Table BPB. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1511, Run 141980901	Tissue Name	Rel. Exp.(%) Ag1511, Run 141980901
Endothelial cells	0.1	Renal ca. 786-0	10.7

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Heart (Fetal)	0.6	Renal ca. A498	9.7
Pancreas	0.3	Renal ca. RXF 393	11.0
Pancreatic ca. CAPAN 2	0.8	Renal ca. ACHN	20.6
Adrenal Gland	14.2	Renal ca. UO-31	26.1
Thyroid	0.8	Renal ca. TK-10	10.6
Salivary gland	27.0	Liver	6.4
Pituitary gland	0.2	Liver (fetal)	1.1
Brain (fetal)	0.0	Liver ca. (hepatoblast) HepG2	6.1
Brain (whole)	0.0	Lung	0.4
Brain (amygdala)	0.2	Lung (fetal)	0.6
Brain (cerebellum)	0.4	Lung ca. (small cell) LX-1	12.2
Brain (hippocampus)	1.8	Lung ca. (small cell) NCI-H69	7.1
Brain (thalamus)	0.9	Lung ca. (s.cell var.) SHP-77	0.0
Cerebral Cortex	1.5	Lung ca. (large cell)NCI-H460	8.6
Spinal cord	0.1	Lung ca. (non-sm. cell) A549	2.7
glio/astro U87-MG	0.0	Lung ca. (non-s.cell) NCI-H23	5.8
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) HOP-62	14.9
astrocytoma SW1783	0.2	Lung ca. (non-s.cl) NCI-H522	0.1
neuro*; met SK-N-AS	0.0	Lung ca. (squam.) SW 900	16.4
astrocytoma SF-539	0.1	Lung ca. (squam.) NCI-H596	4.0
astrocytoma SNB-75	0.0	Mammary gland	6.4
glioma SNB-19	1.1	Breast ca.* (pl.ef) MCF-7	1.2
glioma U251	0.0	Breast ca.* (pl.ef) MDA-MB-231	2.1
glioma SF-295	5.8	Breast ca.* (pl. ef) T47D	9.2
Heart	30.6	Breast ca. BT-549	0.3
Skeletal Muscle	0.8	Breast ca. MDA-N	19.1
Bone marrow	2.8	Ovary	4.2
Thymus	0.1	Ovarian ca. OVCAR-	4.9

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		3	
Spleen	1.0	Ovarian ca. OVCAR-4	23.8
Lymph node	0.5	Ovarian ca. OVCAR-5	23.8
Colorectal Tissue	1.8	Ovarian ca. OVCAR-8	31.9
Stomach	0.7	Ovarian ca. IGROV-1	1.0
Small intestine	6.7	Ovarian ca. (ascites) SK-OV-3	10.6
Colon ca. SW480	1.5	Uterus	0.4
Colon ca.* SW620 (SW480 met)	7.7	Placenta	1.1
Colon ca. HT29	3.0	Prostate	10.4
Colon ca. HCT-116	5.2	Prostate ca.* (bone met) PC-3	14.3
Colon ca. CaCo-2	2.6	Testis	0.3
Colon ca. Tissue (ODO3866)	4.5	Melanoma Hs688(A).T	7.5
Colon ca. HCC-2998	14.3	Melanoma* (met) Hs688(B).T	11.7
Gastric ca.* (liver met) NCI-N87	2.1	Melanoma UACC-62	0.4
Bladder	43.2	Melanoma M14	11.3
Trachea	0.0	Melanoma LOX IMVI	0.0
Kidney	**100.0**	Melanoma* (met) SK-MEL-5	0.0
Kidney (fetal)	13.1		

Table BPC. Panel 2D

Tissue Name	Rel. Exp.(%) Ag1511, Run 145420468	Tissue Name	Rel. Exp.(%) Ag1511, Run 145420468
Normal Colon	16.2	Kidney Margin 8120608	5.9
CC Well to Mod Diff (ODO3866)	3.3	Kidney Cancer 8120613	0.0
CC Margin (ODO3866)	0.0	Kidney Margin 8120614	3.4
CC Gr.2 rectosigmoid (ODO3868)	1.6	Kidney Cancer 9010320	3.5

CC Margin (ODO3868)	1.6	Kidney Margin 9010321	6.7
CC Mod Diff (ODO3920)	6.0	Normal Uterus	5.3
CC Margin (ODO3920)	5.7	Uterus Cancer 064011	36.9
CC Gr.2 ascend colon (ODO3921)	1.9	Normal Thyroid	31.9
CC Margin (ODO3921)	1.8	Thyroid Cancer 064010	34.2
CC from Partial Hepatectomy (ODO4309) Mets	4.2	Thyroid Cancer A302152	12.2
Liver Margin (ODO4309)	0.8	Thyroid Margin A302153	52.5
Colon mets to lung (OD04451-01)	9.5	Normal Breast	42.0
Lung Margin (OD04451-02)	3.0	Breast Cancer (OD04566)	17.8
Normal Prostate 6546-1	14.1	Breast Cancer (OD04590-01)	24.7
Prostate Cancer (OD04410)	12.2	Breast Cancer Mets (OD04590-03)	62.4
Prostate Margin (OD04410)	32.5	Breast Cancer Metastasis (OD04655-05)	47.3
Prostate Cancer (OD04720-01)	27.7	Breast Cancer 064006	15.9
Prostate Margin (OD04720-02)	38.7	Breast Cancer 1024	24.8
Normal Lung 061010	**100.0**	Breast Cancer 9100266	7.6
Lung Met to Muscle (ODO4286)	13.2	Breast Margin 9100265	11.7
Muscle Margin (ODO4286)	3.1	Breast Cancer A209073	47.3
Lung Malignant Cancer (OD03126)	14.6	Breast Margin A2090734	12.9
Lung Margin (OD03126)	9.0	Normal Liver	5.4
Lung Cancer (OD04404)	4.2	Liver Cancer 064003	5.3
Lung Margin (OD04404)	5.2	Liver Cancer 1025	1.8
Lung Cancer (OD04565)	7.4	Liver Cancer 1026	0.0
Lung Margin (OD04565)	23.3	Liver Cancer 6004-T	5.2
Lung Cancer (OD04237-	19.2	Liver Tissue 6004-N	5.2

01)			
Lung Margin (OD04237-02)	3.9	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	31.4	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	3.0	Normal Bladder	29.7
Melanoma Mets to Lung (OD04321)	7.6	Bladder Cancer 1023	4.4
Lung Margin (OD04321)	8.1	Bladder Cancer A302173	11.3
Normal Kidney	93.3	Bladder Cancer (OD04718-01)	6.7
Kidney Ca, Nuclear grade 2 (OD04338)	33.4	Bladder Normal Adjacent (OD04718-03)	5.0
Kidney Margin (OD04338)	24.8	Normal Ovary	0.8
Kidney Ca Nuclear grade 1/2 (OD04339)	85.9	Ovarian Cancer 064008	7.2
Kidney Margin (OD04339)	33.2	Ovarian Cancer (OD04768-07)	8.6
Kidney Ca, Clear cell type (OD04340)	22.5	Ovary Margin (OD04768-08)	4.1
Kidney Margin (OD04340)	40.9	Normal Stomach	8.5
Kidney Ca, Nuclear grade 3 (OD04348)	3.0	Gastric Cancer 9060358	0.6
Kidney Margin (OD04348)	52.9	Stomach Margin 9060359	1.4
Kidney Cancer (OD04622-01)	36.1	Gastric Cancer 9060395	5.7
Kidney Margin (OD04622-03)	19.1	Stomach Margin 9060394	3.0
Kidney Cancer (OD04450-01)	22.8	Gastric Cancer 9060397	5.1
Kidney Margin (OD04450-03)	42.6	Stomach Margin 9060396	1.0
Kidney Cancer 8120607	0.5	Gastric Cancer 064005	15.6

Table BPD. Panel 4D

Tissue Name	Rel. Exp.(%)	Tissue Name	Rel. Exp.(%)

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	Ag1511, Run 146090941		Ag1511, Run 146090941
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	8.4	HUVEC IFN gamma	66.0
Secondary Tr1 act	8.1	HUVEC TNF alpha + IFN gamma	7.2
Secondary Th1 rest	14.7	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	27.2	Lung Microvascular EC none	0.0
Primary Th1 act	4.5	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	5.4	Microvascular Dermal EC none	0.0
Primary Tr1 act	7.7	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	65.1	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	40.3	Small airway epithelium none	0.0
Primary Tr1 rest	17.1	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	7.7	Coronery artery SMC rest	6.6
CD45RO CD4 lymphocyte act	15.9	Coronery artery SMC TNFalpha + IL-1beta	17.4
CD8 lymphocyte act	3.7	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	4.2	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	3.6	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	8.8	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	33.2	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	7.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	10.0	Liver cirrhosis	68.8
LAK cells IL-2+IL-12	6.3	Lupus kidney	17.2
LAK cells IL-2+IFN gamma	3.5	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	4.5	NCI-H292 IL-4	0.0
LAK cells	5.0	NCI-H292 IL-9	0.0

PMA/ionomycin			
NK Cells IL-2 rest	6.6	NCI-H292 IL-13	3.2
Two Way MLR 3 day	14.6	NCI-H292 IFN gamma	10.7
Two Way MLR 5 day	0.0	HPAEC none	12.7
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	12.2
PBMC rest	3.6	Lung fibroblast none	9.0
PBMC PWM	9.5	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	9.2	Lung fibroblast IL-4	3.3
Ramos (B cell) none	0.0	Lung fibroblast IL-9	35.1
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	4.1
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	71.7
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	10.7
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	7.1
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	8.6
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	14.3
Dendritic cells anti-CD40	0.0	IBD Colitis 2	10.2
Monocytes rest	0.0	IBD Crohn's	5.8
Monocytes LPS	0.0	Colon	8.0
Macrophages rest	5.4	Lung	21.5
Macrophages LPS	4.9	Thymus	**100.0**
HUVEC none	0.0	Kidney	33.9
HUVEC starved	0.0		

Panel 1.2 Summary: Ag1511 Expression of the GMAC076959_C gene is highest in a sample derived from normal kidney tissue (CT = 27.4). Other normal tissues that show substantial expression are adrenal gland, salivary gland, heart and bladder. In addition, there is substantial expression in cell lines derived from cancers including colon cancer, renal cancer and ovarian cancer. Thus, the expression of this gene could be used to distinguish normal kidney, adrenal gland, salivary gland, heart and bladder form other samples in the panel. Moreover, therapeutic modulation of this gene, through the use of antibodies, small

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molecule drugs or protein therapeutics might be of use in the treatment of colon, renal or ovarian cancer.

This gene represents a novel G-protein coupled receptor (GPCR) that also shows expression in the brain. The GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and α2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the a-adrenergic receptors have been implicated in memory. Therefore, this gene may be of use as a small molecule target for the treatment of any of the described diseases.

References:

1. El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.)

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reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response. The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at

alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine

5   compared with the SSRIs.

3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic

10   receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of

15   glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently

20   identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9 Related Articles, Books, LinkOut

25   Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly

30   reduced cortical infarct volume as measured 24 h later (30% vs controls, $p < 0.05$). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, $p < 0.05$). Neuroprotective properties of SCH

58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 1.3D Summary: <u>Ag1511</u> Data from this experiment is not included because of a potential problem in one of the wells (data not shown).

5   **Panel 2D Summary:** <u>Ag1511</u> (run# 145420468) Expression of this gene is highest in a sample derived from normal lung tissue (CT = 32). In addition, there is substantial expression associated with normal kidney tissue; this result is consistent with what is observed in Panel 1.2. Of note was the clustered expression associated with kidney derived tissues and prostate derived tissues. Thus, the expression of this gene could be used to distinguish normal lung,

10   kidney or prostate tissue from the other tissues in the panel. Moreover, therapeutic modulation of this gene, through the use of antibodies, small molecule drugs or protein therapeutics might be of use in the treatment of kidney or prostate cancer. <u>Ag1511</u> (run#145017306) This experiment must be discounted due to experimental difficulties (bad amp plot).

15   **Panel 4D Summary:** <u>Ag1511</u> Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

BQ. GMAC076959_D: GPCR

Expression of gene GMAC076959_D was assessed using the primer-probe set

20   Ag1512, described in Table BQA. Results of the RTQ-PCR runs are shown in Tables BQB, BQC, BQD and BQE.

<u>Table BQA</u>. Probe Name Ag1512

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-cttcttctaaggttgccgttct-3'	22	483	543
Probe	TET-5'-ccgggatgtgaaccacctcttctgt-3'-TAMRA	25	512	544
Reverse	5'-gcttgaggacagacagaatttc-3'	22	537	545

<u>Table BQB</u>. CNS_neurodegeneration_v1.0

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Tissue Name	Rel. Exp.(%) Ag1512, Run 207575552	Tissue Name	Rel. Exp.(%) Ag1512, Run 207575552
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	3.0
AD 2 Hippo	1.2	Control (Path) 4 Temporal Ctx	9.4
AD 3 Hippo	0.0	AD 1 Occipital Ctx	9.0
AD 4 Hippo	4.9	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	6.6	AD 3 Occipital Ctx	0.0
AD 6 Hippo	3.2	AD 4 Occipital Ctx	**100.0**
Control 2 Hippo	0.0	AD 5 Occipital Ctx	2.9
Control 4 Hippo	41.5	AD 6 Occipital Ctx	7.1
Control (Path) 3 Hippo	10.7	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	21.8	Control 2 Occipital Ctx	0.0
AD 2 Temporal Ctx	6.0	Control 3 Occipital Ctx	17.3
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	16.5
AD 4 Temporal Ctx	12.4	Control (Path) 1 Occipital Ctx	2.7
AD 5 Inf Temporal Ctx	20.9	Control (Path) 2 Occipital Ctx	0.0
AD 5 Sup Temporal Ctx	22.7	Control (Path) 3 Occipital Ctx	4.2
AD 6 Inf Temporal Ctx	11.0	Control (Path) 4 Occipital Ctx	5.1
AD 6 Sup Temporal Ctx	2.7	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	11.9
Control 2 Temporal Ctx	0.0	Control 3 Parietal Ctx	0.0
Control 3 Temporal Ctx	2.9	Control (Path) 1 Parietal Ctx	0.0
Control 3 Temporal Ctx	11.1	Control (Path) 2 Parietal Ctx	3.8
Control (Path) 1 Temporal Ctx	0.0	Control (Path) 3 Parietal Ctx	14.6
Control (Path) 2 Temporal Ctx	0.0	Control (Path) 4 Parietal Ctx	23.3

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Table BQC. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1512, Run 141962551	Tissue Name	Rel. Exp.(%) Ag1512, Run 141962551
Endothelial cells	0.0	Renal ca. 786-0	24.7
Heart (Fetal)	0.8	Renal ca. A498	9.0
Pancreas	2.3	Renal ca. RXF 393	10.7
Pancreatic ca. CAPAN 2	0.8	Renal ca. ACHN	9.6
Adrenal Gland	5.3	Renal ca. UO-31	24.8
Thyroid	1.2	Renal ca. TK-10	24.3
Salivary gland	36.1	Liver	7.9
Pituitary gland	0.2	Liver (fetal)	1.7
Brain (fetal)	0.0	Liver ca. (hepatoblast) HepG2	2.6
Brain (whole)	0.0	Lung	0.3
Brain (amygdala)	0.9	Lung (fetal)	0.6
Brain (cerebellum)	0.7	Lung ca. (small cell) LX-1	25.5
Brain (hippocampus)	0.7	Lung ca. (small cell) NCI-H69	45.7
Brain (thalamus)	0.9	Lung ca. (s.cell var.) SHP-77	1.2
Cerebral Cortex	1.2	Lung ca. (large cell)NCI-H460	6.0
Spinal cord	0.4	Lung ca. (non-sm. cell) A549	7.7
glio/astro U87-MG	0.0	Lung ca. (non-s.cell) NCI-H23	5.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) HOP-62	10.7
astrocytoma SW1783	1.2	Lung ca. (non-s.cl) NCI-H522	1.8
Neuro*; met SK-N-AS	0.8	Lung ca. (squam.) SW 900	45.7
astrocytoma SF-539	0.7	Lung ca. (squam.) NCI-H596	20.6
astrocytoma SNB-75	0.7	Mammary gland	14.3
glioma SNB-19	4.7	Breast ca.* (pl.ef) MCF-7	7.4
glioma U251	2.5	Breast ca.* (pl.ef) MDA-MB-231	0.9
glioma SF-295	6.3	Breast ca.* (pl. ef)	16.7

		T47D	
Heart	13.4	Breast ca. BT-549	1.0
Skeletal Muscle	2.5	Breast ca. MDA-N	21.8
Bone marrow	0.4	Ovary	2.3
Thymus	0.0	Ovarian ca. OVCAR-3	11.9
Spleen	0.4	Ovarian ca. OVCAR-4	22.1
Lymph node	0.2	Ovarian ca. OVCAR-5	42.6
Colorectal Tissue	5.2	Ovarian ca. OVCAR-8	54.7
Stomach	3.1	Ovarian ca. IGROV-1	4.6
Small intestine	7.0	Ovarian ca. (ascites) SK-OV-3	8.6
Colon ca. SW480	1.7	Uterus	5.3
Colon ca.* SW620 (SW480 met)	10.0	Placenta	0.7
Colon ca. HT29	12.5	Prostate	17.8
Colon ca. HCT-116	12.9	Prostate ca.* (bone met) PC-3	12.0
Colon ca. CaCo-2	4.4	Testis	0.3
Colon ca. Tissue (ODO3866)	12.9	Melanoma Hs688(A).T	2.4
Colon ca. HCC-2998	64.6	Melanoma* (met) Hs688(B).T	14.5
Gastric ca.* (liver met) NCI-N87	6.7	Melanoma UACC-62	0.0
Bladder	47.6	Melanoma M14	38.4
Trachea	1.0	Melanoma LOX IMVI	0.0
Kidney	**100.0**	Melanoma* (met) SK-MEL-5	0.0
Kidney (fetal)	6.5		

Table BQD. Panel 2D

Tissue Name	Rel. Exp.(%) Ag1512, Run 144873351	Tissue Name	Rel. Exp.(%) Ag1512, Run 144873351
Normal Colon	41.5	Kidney Margin 8120608	2.0

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CC Well to Mod Diff (ODO3866)	10.8	Kidney Cancer 8120613	0.5
CC Margin (ODO3866)	4.4	Kidney Margin 8120614	4.3
CC Gr.2 rectosigmoid (ODO3868)	4.1	Kidney Cancer 9010320	2.0
CC Margin (ODO3868)	0.0	Kidney Margin 9010321	5.6
CC Mod Diff (ODO3920)	8.8	Normal Uterus	1.4
CC Margin (ODO3920)	14.4	Uterus Cancer 064011	18.2
CC Gr.2 ascend colon (ODO3921)	3.6	Normal Thyroid	15.2
CC Margin (ODO3921)	4.1	Thyroid Cancer 064010	31.9
CC from Partial Hepatectomy (ODO4309) Mets	16.5	Thyroid Cancer A302152	8.8
Liver Margin (ODO4309)	3.1	Thyroid Margin A302153	37.4
Colon mets to lung (OD04451-01)	2.8	Normal Breast	53.2
Lung Margin (OD04451-02)	3.0	Breast Cancer (OD04566)	13.5
Normal Prostate 6546-1	17.4	Breast Cancer (OD04590-01)	16.7
Prostate Cancer (OD04410)	11.2	Breast Cancer Mets (OD04590-03)	9.6
Prostate Margin (OD04410)	21.0	Breast Cancer Metastasis (OD04655-05)	11.3
Prostate Cancer (OD04720-01)	20.9	Breast Cancer 064006	11.2
Prostate Margin (OD04720-02)	17.0	Breast Cancer 1024	14.7
Normal Lung 061010	14.9	Breast Cancer 9100266	1.2
Lung Met to Muscle (ODO4286)	0.6	Breast Margin 9100265	6.6
Muscle Margin (ODO4286)	0.0	Breast Cancer A209073	20.7
Lung Malignant Cancer (OD03126)	18.0	Breast Margin A2090734	27.0

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Lung Margin (OD03126)	5.8	Normal Liver	7.7
Lung Cancer (OD04404)	12.2	Liver Cancer 064003	5.4
Lung Margin (OD04404)	14.6	Liver Cancer 1025	3.5
Lung Cancer (OD04565)	2.6	Liver Cancer 1026	0.0
Lung Margin (OD04565)	2.4	Liver Cancer 6004-T	3.8
Lung Cancer (OD04237-01)	46.3	Liver Tissue 6004-N	6.7
Lung Margin (OD04237-02)	3.7	Liver Cancer 6005-T	0.8
Ocular Mel Met to Liver (ODO4310)	2.8	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	0.9	Normal Bladder	11.3
Melanoma Mets to Lung (OD04321)	2.3	Bladder Cancer 1023	1.2
Lung Margin (OD04321)	13.2	Bladder Cancer A302173	12.8
Normal Kidney	**100.0**	Bladder Cancer (OD04718-01)	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	22.8	Bladder Normal Adjacent (OD04718-03)	2.1
Kidney Margin (OD04338)	28.5	Normal Ovary	0.5
Kidney Ca Nuclear grade 1/2 (OD04339)	25.2	Ovarian Cancer 064008	2.9
Kidney Margin (OD04339)	35.1	Ovarian Cancer (OD04768-07)	17.8
Kidney Ca, Clear cell type (OD04340)	13.9	Ovary Margin (OD04768-08)	2.1
Kidney Margin (OD04340)	34.9	Normal Stomach	10.3
Kidney Ca, Nuclear grade 3 (OD04348)	0.8	Gastric Cancer 9060358	0.0
Kidney Margin (OD04348)	31.2	Stomach Margin 9060359	1.9
Kidney Cancer (OD04622-01)	22.2	Gastric Cancer 9060395	4.0
Kidney Margin (OD04622-03)	2.6	Stomach Margin 9060394	4.5
Kidney Cancer (OD04450-01)	11.7	Gastric Cancer 9060397	11.7
Kidney Margin (OD04450-03)	25.9	Stomach Margin 9060396	0.0

Kidney Cancer 8120607	0.0	Gastric Cancer 064005	3.8

Table BQE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1512, Run 146090942	Tissue Name	Rel. Exp.(%) Ag1512, Run 146090942
Secondary Th1 act	1.8	HUVEC IL-1beta	0.0
Secondary Th2 act	9.4	HUVEC IFN gamma	9.5
Secondary Tr1 act	3.8	HUVEC TNF alpha + IFN gamma	19.2
Secondary Th1 rest	5.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	2.0	HUVEC IL-11	0.0
Secondary Tr1 rest	4.5	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	3.6	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	14.3	Bronchial epithelium TNFalpha + IL1beta	4.2
Primary Th2 rest	7.2	Small airway epithelium none	1.9
Primary Tr1 rest	7.2	Small airway epithelium TNFalpha + IL-1beta	24.0
CD45RA CD4 lymphocyte act	2.4	Coronery artery SMC rest	12.7
CD45RO CD4 lymphocyte act	8.2	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	2.0	KU-812 (Basophil) rest	1.6
CD4 lymphocyte none	1.6	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	4.2	CCD1106 (Keratinocytes) none	0.7
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	3.6
LAK cells IL-2	1.9	Liver cirrhosis	42.6

LAK cells IL-2+IL-12	0.9	Lupus kidney	9.7
LAK cells IL-2+IFN gamma	3.9	NCI-H292 none	25.9
LAK cells IL-2+ IL-18	1.5	NCI-H292 IL-4	47.6
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	34.2
NK Cells IL-2 rest	2.6	NCI-H292 IL-13	4.9
Two Way MLR 3 day	7.0	NCI-H292 IFN gamma	15.4
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	6.1	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	12.0
PBMC PWM	10.6	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	6.0	Lung fibroblast IL-4	18.9
Ramos (B cell) none	0.0	Lung fibroblast IL-9	10.1
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	16.5
B lymphocytes PWM	9.3	Lung fibroblast IFN gamma	18.7
B lymphocytes CD40L and IL-4	14.3	Dermal fibroblast CCD1070 rest	1.8
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	5.1
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	2.6
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.5	Dermal fibroblast IL-4	5.9
Dendritic cells anti-CD40	0.0	IBD Colitis 2	6.7
Monocytes rest	0.0	IBD Crohn's	12.0
Monocytes LPS	0.0	Colon	19.8
Macrophages rest	0.0	Lung	8.0
Macrophages LPS	0.0	Thymus	**100.0**
HUVEC none	0.0	Kidney	18.8
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag1512 No difference in the expression of this gene was detected in the postmortem brains of Alzheimer's diseased patients when compared to controls; however this panel demonstrates the expression of this gene in the brains of an

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independent group of subjects. See Panel 1.3D for a discussion of the potential utility in treatment of central nervous system diseases.

Panel 1.2 Summary: <u>Ag1512</u> Expression of the GMAC076959_D gene is highest in a sample derived from normal adult kidney tissue (CT=28.1). This observation is consistent with what is observed in Panel 2D. Of particular interest is the difference in expression of this gene in adult kidney (CT = 28) versus fetal kidney (CT = 32). Thus, the expression of this gene could be used to distinguish adult kidney from fetal kidney tissue. In addition, there is substantial expression of this gene in a number of other normal tissues, including prostate, mammary gland, bladder, heart and salivary gland. Therefore, expression of this gene could be used to distinguish these samples from other samples in the panel. In addition, there appears to be substantial GMAC076959_D gene expression in samples derived from a number of cancer cell lines, including colon, renal, lung and ovarian cancer cell lines. Therapeutic modulation of this gene or its protein product, through the use of antibodies, small molecule drugs or protein therapeutics, might be of benefit in the treatment of colon, renal, lung or ovarian cancer.

This gene represents a novel G-protein coupled receptor (GPCR) that also shows low expression in the brain. The GPCR family of receptors contains a large number of neurotransmitter receptors, including the dopamine, serotonin, α and β-adrenergic, acetylcholine muscarinic, histamine, peptide, and metabotropic glutamate receptors. GPCRs are excellent drug targets in various neurologic and psychiatric diseases. All antipsychotics have been shown to act at the dopamine D2 receptor; similarly novel antipsychotics also act at the serotonergic receptor, and often the muscarinic and adrenergic receptors as well. While the majority of antidepressants can be classified as selective serotonin reuptake inhibitors, blockade of the 5-HT1A and α2 adrenergic receptors increases the effects of these drugs. The GPCRs are also of use as drug targets in the treatment of stroke. Blockade of the glutamate receptors may decrease the neuronal death resulting from excitotoxicity; further more the purinergic receptors have also been implicated as drug targets in the treatment of cerebral ischemia. The β-adrenergic receptors have been implicated in the treatment of ADHD with Ritalin, while the a-adrenergic receptors have been implicated in memory. Therefore this gene may be of use as a small molecule target for the treatment of any of the described diseases.

El Yacoubi M, Ledent C, Parmentier M, Bertorelli R, Ongini E, Costentin J, Vaugeois JM. Adenosine A2A receptor antagonists are potential antidepressants: evidence based on pharmacology and A2A receptor knockout mice. Br J Pharmacol 2001 Sep;134(1):68-77

1. Adenosine, an ubiquitous neuromodulator, and its analogues have been shown to produce 'depressant' effects in animal models believed to be relevant to depressive disorders, while adenosine receptor antagonists have been found to reverse adenosine-mediated 'depressant' effect. 2. We have designed studies to assess whether adenosine A2A receptor antagonists, or genetic inactivation of the receptor would be effective in established screening procedures, such as tail suspension and forced swim tests, which are predictive of clinical antidepressant activity. 3. Adenosine A2A receptor knockout mice were found to be less sensitive to 'depressant' challenges than their wildtype littermates. Consistently, the adenosine A2A receptor blockers SCH 58261 (1 - 10 mg kg(-1), i.p.) and KW 6002 (0.1 - 10 mg kg(-1), p.o.) reduced the total immobility time in the tail suspension test. 4. The efficacy of adenosine A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg(-1)) and ZM 241385 (15 - 60 mg kg(-1)) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg(-1) reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg(-1) reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg(-1) by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg(-1) i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg(-1) i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT1A (cell body) and 5-HT1B (terminal) autoreceptors, which,

respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT1 autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT1A receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response. The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha1-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha2-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at alpha2-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. Expert Opin Investig Drugs 1999 Nov;8(11):1837-1848

The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist. Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

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Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. Neuroreport 1998 Dec 1;9(17):3955-9

Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, p < 0.05). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, p < 0.05). Neuroprotective properties of SCH 58261 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 2D Summary: Ag1512 Expression of the GMAC076959_D gene is highest in a sample derived from normal kidney (CT = 30). In addition, there is substantial expression of this gene in normal breast and normal colon. Of particular note is the fact that there appears to be substantial differences in expression between a number of kidney cancers and their respective normal adjacent controls. Thus, the expression of this gene could be used to distinguish normal kidney from the other tissues in the panel. Moreover, therapeutic modulation of this gene, through the use of antibodies, small molecule drugs or protein therapeutics, might be of benefit in the treatment of kidney cancer.

Panel 4D Summary: Ag1512 The GMAC076959_D gene is expressed in the thymus, cirrhotic liver and small airway epithelium. Normal liver does express this transcript in panel 1.2 and 2D. Thus, the transcript or the protein encoded for by the transcript could be used diagnostically to identify inflamed small airway epithelium, liver and thymus. In addition, the protein encoded by this transcript could be used to design therapeutics to treat inflammation of the airway epithelium in asthma and COPD.

BR. GMAP000818_A_3/CG143590-01: Olfactory Receptor

Expression of gene GMAP000818_A_3 (also known as CG143590-01) was assessed using the primer-probe set Ag1517, described in Table BRA. Results of the RTQ-PCR runs are shown in Table BRB.

Table BRA. Probe Name Ag1517

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ctcatgaatctggtaggaccaa-3'	22	834	546
Probe	TET-5'-tgctgaaccctttgatctataccttgagg-3'-TAMRA	29	856	547
Reverse	5'-cctgtcctgtgcaatattgttt-3'	22	910	548

5   Table BRB. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1517, Run 141990530	Tissue Name	Rel. Exp.(%) Ag1517, Run 141990530
Endothelial cells	0.0	Renal ca. 786-0	0.0
Heart (Fetal)	0.0	Renal ca. A498	0.0
Pancreas	0.0	Renal ca. RXF 393	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. ACHN	0.3
Adrenal Gland	0.0	Renal ca. UO-31	1.2
Thyroid	0.0	Renal ca. TK-10	0.0
Salivary gland	0.0	Liver	0.0
Pituitary gland	0.0	Liver (fetal)	0.0
Brain (fetal)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (whole)	0.0	Lung	0.0
Brain (amygdala)	0.3	Lung (fetal)	0.0
Brain (cerebellum)	0.2	Lung ca. (small cell) LX-1	0.4
Brain (hippocampus)	0.4	Lung ca. (small cell) NCI-H69	7.6
Brain (thalamus)	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Cerebral Cortex	0.0	Lung ca. (large cell)NCI-H460	1.1
Spinal cord	0.0	Lung ca. (non-sm. cell) A549	2.5
glio/astro U87-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0

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glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) HOP-62	3.6
astrocytoma SW1783	0.9	Lung ca. (non-s.cl) NCI-H522	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (squam.) SW 900	0.9
astrocytoma SF-539	0.8	Lung ca. (squam.) NCI-H596	2.5
astrocytoma SNB-75	0.2	Mammary gland	0.2
glioma SNB-19	2.1	Breast ca.* (pl.ef) MCF-7	33.4
glioma U251	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
glioma SF-295	4.0	Breast ca.* (pl. ef) T47D	97.3
Heart	0.0	Breast ca. BT-549	0.9
Skeletal Muscle	0.4	Breast ca. MDA-N	1.7
Bone marrow	0.0	Ovary	0.0
Thymus	0.0	Ovarian ca. OVCAR-3	0.0
Spleen	0.0	Ovarian ca. OVCAR-4	0.9
Lymph node	0.0	Ovarian ca. OVCAR-5	15.7
Colorectal Tissue	0.8	Ovarian ca. OVCAR-8	0.6
Stomach	0.0	Ovarian ca. IGROV-1	0.0
Small intestine	0.0	Ovarian ca. (ascites) SK-OV-3	0.7
Colon ca. SW480	0.0	Uterus	0.0
Colon ca.* SW620 (SW480 met)	0.0	Placenta	3.4
Colon ca. HT29	1.9	Prostate	0.0
Colon ca. HCT-116	0.0	Prostate ca.* (bone met) PC-3	42.9
Colon ca. CaCo-2	0.0	Testis	1.1
Colon ca. Tissue (ODO3866)	1.7	Melanoma Hs688(A).T	0.0
Colon ca. HCC-2998	0.2	Melanoma* (met) Hs688(B).T	1.4
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma UACC-62	**100.0**

Bladder	3.3	Melanoma M14	5.0
Trachea	0.0	Melanoma LOX IMVI	0.0
Kidney	1.8	Melanoma* (met) SK-MEL-5	0.0
Kidney (fetal)	0.0		

Panel 1.2 Summary: <u>Ag1517</u> Expression of this gene appears to be primarily associated with cell lines derived from cancer tissue. These include a lung cancer, two breast cancer cell lines, one ovarian cancer, one prostate cancer and one melanoma cell line. Thus, the expression of this gene could be used to distinguish the above cell lines from the other samples on this panel. Morover, therepeutic modulation of this gene or its protein product, through the use of antibodies, small molecule drugs or protein therapeutics, might be of use for the treatment of lung cancer, breast cancer, ovarian cancer, prostate cancer or melanoma.

BS. GM524k20_A: Olfactory Receptor

Expression of gene GM524k20_A was assessed using the primer-probe set Ag1502, described in Table BSA. Results of the RTQ-PCR runs are shown in Table BSB.

<u>Table BSA</u>. Probe Name Ag1502

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-atgatggcttatgaccattacg-3'	22	372	549
Probe	TET-5'-cccttgttgtatacagtcattatggccca-3'-TAMRA	29	408	550
Reverse	5'-taagaagcaaggaccatctgaa-3'	22	448	551

<u>Table BSB</u>. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1502, Run 141890038	Tissue Name	Rel. Exp.(%) Ag1502, Run 141890038
Endothelial cells	0.0	Renal ca. 786-0	0.0
Heart (Fetal)	0.0	Renal ca. A498	5.6
Pancreas	0.0	Renal ca. RXF 393	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. ACHN	2.2
Adrenal Gland	0.0	Renal ca. UO-31	4.2

Thyroid	0.0	Renal ca. TK-10	1.0
Salivary gland	0.0	Liver	0.0
Pituitary gland	0.0	Liver (fetal)	0.0
Brain (fetal)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (whole)	0.0	Lung	0.0
Brain (amygdala)	0.0	Lung (fetal)	0.0
Brain (cerebellum)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (hippocampus)	0.0	Lung ca. (small cell) NCI-H69	49.3
Brain (thalamus)	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Cerebral Cortex	0.0	Lung ca. (large cell)NCI-H460	7.4
Spinal cord	0.0	Lung ca. (non-sm. cell) A549	4.1
glio/astro U87-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) HOP-62	17.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cl) NCI-H522	7.2
neuro*; met SK-N-AS	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) NCI-H596	27.2
astrocytoma SNB-75	0.0	Mammary gland	0.0
glioma SNB-19	4.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MDA-MB-231	1.5
glioma SF-295	3.6	Breast ca.* (pl. ef) T47D	58.6
Heart	0.0	Breast ca. BT-549	10.4
Skeletal Muscle	0.0	Breast ca. MDA-N	23.2
Bone marrow	0.0	Ovary	0.0
Thymus	0.0	Ovarian ca. OVCAR-3	4.7
Spleen	0.0	Ovarian ca. OVCAR-4	0.0
Lymph node	0.0	Ovarian ca. OVCAR-5	**100.0**

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Colorectal Tissue	10.2	Ovarian ca. OVCAR-8	2.0
Stomach	0.0	Ovarian ca. IGROV-1	3.4
Small intestine	0.0	Ovarian ca. (ascites) SK-OV-3	0.0
Colon ca. SW480	0.0	Uterus	0.0
Colon ca.* SW620 (SW480 met)	0.0	Placenta	0.0
Colon ca. HT29	7.7	Prostate	0.0
Colon ca. HCT-116	0.0	Prostate ca.* (bone met) PC-3	8.5
Colon ca. CaCo-2	0.0	Testis	0.0
Colon ca. Tissue (ODO3866)	17.1	Melanoma Hs688(A).T	3.8
Colon ca. HCC-2998	0.0	Melanoma* (met) Hs688(B).T	18.7
Gastric ca.* (liver met) NCI-N87	3.4	Melanoma UACC-62	6.6
Bladder	11.0	Melanoma M14	17.7
Trachea	0.0	Melanoma LOX IMVI	0.0
Kidney	0.0	Melanoma* (met) SK-MEL-5	1.6
Kidney (fetal)	0.0		

Panel 1.2 Summary: Ag1502 Expression of the GM524k20_A gene is highest in an ovarian cancer cell line (CT=31.7). Significant expression is also seen in cell lines derived from breast cancer, lung cancer and melanoma. Thus, the expression of this gene could be used to distinguish the above cell lines from the other samples on this panel. Morover, therepeutic modulation of this gene or its protein product, through the use of antibodies, small molecule drugs or protein therapeutics, might be of use for the treatment of lung cancer, breast cancer, ovarian cancer, or melanoma.

BT. GM563n7_A/CG55830-04: Olfactory Receptor

Expression of gene GM563n7_A (also known as CG55830-04) was assessed using the primer-probe set Ag1394, described in Table BTA. Results of the RTQ-PCR runs are shown in Tables BTB, BTC, BTD and BTE.

Table BTA. Probe Name Ag1394

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tccagctagactctcaccttca-3'	22	74	552
Probe	TET-5'-cttagccacttggccctcactgacat-3'-TAMRA	26	115	553
Reverse	5'-ggacagtgacagatgaaaagga-3'	22	142	554

Table BTB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag1394, Run 207567587	Tissue Name	Rel. Exp.(%) Ag1394, Run 207567587
AD 1 Hippo	2.7	Control (Path) 3 Temporal Ctx	6.4
AD 2 Hippo	1.9	Control (Path) 4 Temporal Ctx	5.9
AD 3 Hippo	0.0	AD 1 Occipital Ctx	4.4
AD 4 Hippo	0.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	28.5	AD 3 Occipital Ctx	1.9
AD 6 Hippo	33.4	AD 4 Occipital Ctx	10.6
Control 2 Hippo	11.0	AD 5 Occipital Ctx	0.0
Control 4 Hippo	9.8	AD 6 Occipital Ctx	0.0
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	2.5
AD 1 Temporal Ctx	3.7	Control 2 Occipital Ctx	14.2
AD 2 Temporal Ctx	0.0	Control 3 Occipital Ctx	33.0
AD 3 Temporal Ctx	32.3	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	6.2	Control (Path) 1 Occipital Ctx	**100.0**
AD 5 Inf Temporal Ctx	32.8	Control (Path) 2 Occipital Ctx	20.0
AD 5 Sup Temporal Ctx	47.6	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	18.8	Control (Path) 4 Occipital Ctx	35.4
AD 6 Sup Temporal Ctx	12.3	Control 1 Parietal Ctx	3.6
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	6.7
Control 2 Temporal	0.0	Control 3 Parietal	0.0

Ctx		Ctx	
Control 3 Temporal Ctx	3.5	Control (Path) 1 Parietal Ctx	56.3
Control 3 Temporal Ctx	2.0	Control (Path) 2 Parietal Ctx	13.8
Control (Path) 1 Temporal Ctx	28.9	Control (Path) 3 Parietal Ctx	13.7
Control (Path) 2 Temporal Ctx	12.0	Control (Path) 4 Parietal Ctx	47.6

Table BTC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag1394, Run 216587327	Tissue Name	Rel. Exp.(%) Ag1394, Run 216587327
Adipose	0.0	Renal ca. TK-10	53.2
Melanoma* Hs688(A).T	35.1	Bladder	8.9
Melanoma* Hs688(B).T	5.8	Gastric ca. (liver met.) NCI-N87	1.7
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	1.0	Colon ca. SW-948	1.8
Melanoma* SK-MEL-5	2.8	Colon ca. SW480	24.8
Squamous cell carcinoma SCC-4	0.3	Colon ca.* (SW480 met) SW620	19.8
Testis Pool	15.0	Colon ca. HT29	0.2
Prostate ca.* (bone met) PC-3	0.2	Colon ca. HCT-116	0.5
Prostate Pool	2.5	Colon ca. CaCo-2	0.6
Placenta	2.0	Colon cancer tissue	11.5
Uterus Pool	0.7	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	5.5	Colon ca. SW-48	0.4
Ovarian ca. OVCAR-4	2.1	Colon Pool	3.0
Ovarian ca. OVCAR-5	33.9	Small Intestine Pool	1.9
Ovarian ca. IGROV-1	2.6	Stomach Pool	6.8
Ovarian ca. OVCAR-8	5.6	Bone Marrow Pool	0.8

Ovary	0.0	Fetal Heart	0.0
Breast ca. MCF-7	10.4	Heart Pool	0.0
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	4.8
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.0
Breast ca. T47D	36.1	Skeletal Muscle Pool	1.2
Breast ca. MDA-N	0.3	Spleen Pool	1.9
Breast Pool	3.6	Thymus Pool	10.3
Trachea	1.6	CNS cancer (glio/astro) U87-MG	19.3
Lung	0.0	CNS cancer (glio/astro) U-118-MG	3.3
Fetal Lung	0.0	CNS cancer (neuro;met) SK-N-AS	2.8
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	90.8	CNS cancer (astro) SNB-75	1.2
Lung ca. NCI-H146	9.5	CNS cancer (glio) SNB-19	6.9
Lung ca. SHP-77	7.5	CNS cancer (glio) SF-295	2.8
Lung ca. A549	19.1	Brain (Amygdala) Pool	0.3
Lung ca. NCI-H526	0.9	Brain (cerebellum)	0.0
Lung ca. NCI-H23	73.2	Brain (fetal)	0.0
Lung ca. NCI-H460	8.6	Brain (Hippocampus) Pool	1.7
Lung ca. HOP-62	0.5	Cerebral Cortex Pool	4.3
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	2.1
Liver	0.0	Brain (Thalamus) Pool	10.0
Fetal Liver	0.6	Brain (whole)	1.6
Liver ca. HepG2	0.7	Spinal Cord Pool	1.0
Kidney Pool	2.1	Adrenal Gland	0.0
Fetal Kidney	0.0	Pituitary gland Pool	1.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	2.5	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	18.8
Renal ca. UO-31	0.0	Pancreas Pool	100.0

Table BTD. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1394, Run 135109479	Rel. Exp.(%) Ag1394, Run 138253119	Tissue Name	Rel. Exp.(%) Ag1394, Run 135109479	Rel. Exp.(%) Ag1394, Run 138253119
Endothelial cells	11.4	4.5	Renal ca. 786-0	0.5	0.0
Heart (Fetal)	0.0	0.7	Renal ca. A498	5.1	3.1
Pancreas	0.9	0.0	Renal ca. RXF 393	2.2	0.4
Pancreatic ca. CAPAN 2	2.4	5.0	Renal ca. ACHN	0.1	0.0
Adrenal Gland	1.2	0.0	Renal ca. UO-31	0.8	0.0
Thyroid	0.0	0.0	Renal ca. TK-10	35.4	49.7
Salivary gland	17.4	1.7	Liver	1.0	1.4
Pituitary gland	1.7	0.0	Liver (fetal)	1.1	1.0
Brain (fetal)	0.1	0.0	Liver ca. (hepatoblast) HepG2	3.6	0.0
Brain (whole)	1.2	0.0	Lung	0.0	0.0
Brain (amygdala)	0.8	0.0	Lung (fetal)	0.4	0.0
Brain (cerebellum)	0.6	0.0	Lung ca. (small cell) LX-1	**100.0**	**100.0**
Brain (hippocampus)	3.8	2.6	Lung ca. (small cell) NCI-H69	23.5	19.3
Brain (thalamus)	1.6	0.0	Lung ca. (s.cell var.) SHP-77	3.7	3.3
Cerebral Cortex	2.7	1.4	Lung ca. (large cell)NCI-H460	18.4	8.1
Spinal cord	0.8	0.0	Lung ca. (non-sm. cell) A549	24.7	27.4
glio/astro U87-MG	38.7	19.5	Lung ca. (non-s.cell) NCI-H23	35.1	33.7
glio/astro U-118-MG	4.8	0.0	Lung ca. (non-s.cell) HOP-62	1.0	1.8
astrocytoma SW1783	0.8	0.4	Lung ca. (non-s.cl) NCI-H522	0.0	0.0
neuro*; met SK-	7.4	1.5	Lung ca.	1.5	0.0

N-AS			(squam.) SW 900		
astrocytoma SF-539	2.5	0.0	Lung ca. (squam.) NCI-H596	6.1	2.9
astrocytoma SNB-75	0.2	0.2	Mammary gland	3.0	2.1
glioma SNB-19	7.6	1.0	Breast ca.* (pl.ef) MCF-7	19.8	2.3
Glioma U251	0.0	0.7	Breast ca.* (pl.ef) MDA-MB-231	0.0	0.0
glioma SF-295	0.8	0.0	Breast ca.* (pl. ef) T47D	5.8	12.4
Heart	0.8	0.0	Breast ca. BT-549	8.3	1.0
Skeletal Muscle	0.0	0.0	Breast ca. MDA-N	3.2	3.0
Bone marrow	2.3	2.7	Ovary	0.0	0.0
Thymus	0.3	0.0	Ovarian ca. OVCAR-3	1.1	0.0
Spleen	4.5	1.0	Ovarian ca. OVCAR-4	3.7	5.8
Lymph node	3.3	1.0	Ovarian ca. OVCAR-5	50.3	54.0
Colorectal Tissue	1.5	1.2	Ovarian ca. OVCAR-8	84.7	24.8
Stomach	7.4	0.5	Ovarian ca. IGROV-1	26.1	10.4
Small intestine	1.7	1.4	Ovarian ca. (ascites) SK-OV-3	12.1	11.4
Colon ca. SW480	3.2	3.5	Uterus	0.8	0.3
Colon ca.* SW620 (SW480 met)	33.0	14.7	Placenta	7.2	0.0
Colon ca. HT29	2.5	1.6	Prostate	2.4	3.3
Colon ca. HCT-116	0.8	0.0	Prostate ca.* (bone met) PC-3	0.8	0.0
Colon ca. CaCo-2	0.6	0.0	Testis	0.9	1.6
Colon ca. Tissue	8.1	7.7	Melanoma	6.6	12.0

(ODO3866)			Hs688(A).T		
Colon ca. HCC-2998	4.7	1.7	Melanoma* (met) Hs688(B).T	9.7	9.3
Gastric ca.* (liver met) NCI-N87	4.8	0.0	Melanoma UACC-62	2.0	2.4
Bladder	14.7	15.8	Melanoma M14	6.8	9.2
Trachea	0.4	0.2	Melanoma LOX IMVI	0.1	0.0
Kidney	7.0	0.4	Melanoma* (met) SK-MEL-5	1.5	2.0
Kidney (fetal)	0.7	0.0			

Table BTE. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag1394, Run 195476582	Tissue Name	Rel. Exp.(%) Ag1394, Run 195476582
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	5.9	HUVEC IFN gamma	0.9
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.7
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	1.3
Secondary Th2 rest	0.0	HUVEC IL-11	1.5
Secondary Tr1 rest	0.9	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.8	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	2.1	Coronery artery SMC rest	0.0
CD45RO CD4	5.1	Coronery artery SMC	0.0

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lymphocyte act		TNFalpha + IL-1beta	
CD8 lymphocyte act	1.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	2.7	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.3
CD4 lymphocyte none	0.6	KU-812 (Basophil) PMA/ionomycin	1.1
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.8	NCI-H292 none	1.5
LAK cells IL-2+IFN gamma	0.0	NCI-H292 IL-4	0.0
LAK cells IL-2+ IL-18	2.1	NCI-H292 IL-9	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-13	0.8
NK Cells IL-2 rest	0.9	NCI-H292 IFN gamma	0.4
Two Way MLR 3 day	0.0	HPAEC none	0.0
Two Way MLR 5 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
Two Way MLR 7 day	0.0	Lung fibroblast none	2.5
PBMC rest	0.0	Lung fibroblast TNF alpha + IL-1 beta	2.5
PBMC PWM	0.7	Lung fibroblast IL-4	0.9
PBMC PHA-L	2.8	Lung fibroblast IL-9	5.1
Ramos (B cell) none	0.0	Lung fibroblast IL-13	3.9
Ramos (B cell) ionomycin	0.0	Lung fibroblast IFN gamma	4.9
B lymphocytes PWM	0.0	Dermal fibroblast CCD1070 rest	0.4
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 TNF alpha	3.3
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 IL-1 beta	2.5
EOL-1 dbcAMP PMA/ionomycin	1.9	Dermal fibroblast IFN gamma	13.0
Dendritic cells none	0.0	Dermal fibroblast IL-4	15.8
Dendritic cells LPS	0.0	Dermal Fibroblasts rest	7.7
Dendritic cells anti-CD40	0.5	Neutrophils TNFa+LPS	2.8

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Monocytes rest	0.0	Neutrophils rest	3.8
Monocytes LPS	0.0	Colon	1.8
Macrophages rest	0.3	Lung	1.4
Macrophages LPS	0.0	Thymus	8.5
HUVEC none	2.9	Kidney	**100.0**
HUVEC starved	1.8		

CNS_neurodegeneration_v1.0 Summary: Ag1394 Expression of this gene is limited to the occipital cortex from the brain of a control patient (CT=34.3).

General_screening_panel_v1.4 Summary: Ag1394 Expression of the GM563n7_A gene is highest in a sample derived from a pool of normal pancreas tissues (CT = 30.9). In addition, there is substantial expression of this gene in samples derived from lung cancer cell lines, breast cancer cell lines, brain cancer cell lines, colon cancer cell lines, an ovarian cancer cell line, a melanoma cell line and testis tissue. Thus, the expression of this gene could be used to distinguish these samples from other samples in the panel. Moreover, therapeutic modulation of this gene or its protein product, through the use of small molecule drugs, antibodies or protein therapeutics, might be of benefit in the treatment of lung cancer, breast cancer, brain cancer, colon cancer ovarian cancer or melanoma. In addition, expression of this gene in pancreas suggests that it may play a role in the development of metabolic diseases, such as diabetes and obesity.

Panel 1.2 Summary: Ag1394 Results from two experiments using the same probe/primer set are reasonably concordant. Low to moderate expression of the GM563n7_A gene is detected in a number of normal tissues on this panel, including endothelial cells, salivary gland, bone marrow, colon, small intestine, bladder, mammary gland, and prostate.

In addition, the GM563n7_A gene is expressed at low levels in the hippocampus and cerebral cortex. The GM563n7_A gene encodes a putative GPCR. Several neurotransmitter receptors are GPCRs, including the dopamine receptor family, the serotonin receptor family, the GABAB receptor, muscarinic acetylcholine receptors, and others; thus this GPCR may represent a novel neurotransmitter receptor. Targeting various neurotransmitter receptors (dopamine, serotonin) has proven to be an effective therapy in psychiatric illnesses such as schizophrenia, bipolar disorder, and depression. Furthermore, the cerebral cortex and hippocampus are regions of the brain that are known to be involved in Alzheimer's disease,

seizure disorders, and in the normal process of memory formation. Therefore, therapeutic modulation of this gene or its protein product may be beneficial in the treatment of one or more of these diseases, as may stimulation and/or blockade of the receptor coded for by the gene. Levels of this gene are higher, however, in areas outside of the central nervous system

5   such as the kidneys and bladder, suggesting the possibility of a wider role in intercellular signaling.

Of further note is the clustered expression of the GM563n7_A gene in cell lines derived from lung cancer, ovarian cancer and melanoma. In fact, this gene is most highly expressed in a sample from a lung cancer cell line (LX-1) among the samples on this panel.

10   In addition, GM563n7_A gene expression is also associated with assorted cell lines from renal cancer and brain cancers. Thus, therapeutic modulation of the activity of the GM563n7_A gene product, through small molecule drugs or antibodies, may be of utility in the treatment of lung cancer, ovarian cancer or melanoma.

General References:

15   1. Hebert TE, Bouvier M. (1998) Structural and functional aspects of G protein-coupled receptor oligomerization. Biochem Cell Biol 76: 1-11.

G protein-coupled receptors (GPCRs) represent the single largest family of cell surface receptors involved in signal transduction. It is estimated that several hundred distinct members of this receptor family in humans direct responses to a wide variety of chemical

20   transmitters, including biogenic amines, amino acids, peptides, lipids, nucleosides, and large polypeptides. These transmembrane receptors are key controllers of such diverse physiological processes as neurotransmission, cellular metabolism, secretion, cellular differentiation, and growth as well as inflammatory and immune responses. GPCRs therefore represent major targets for the development of new drug candidates with potential application

25   in all clinical fields. Many currently used therapeutics act by either activating (agonists) or blocking (antagonists) GPCRs. Studies over the past two decades have provided a wealth of information on the biochemical events underlying cellular signalling by GPCRs. However, our understanding of the molecular interactions between ligands and the receptor protein and, particularly, of the structural correlates of receptor activation or inhibition by agonists and

30   inverse agonists, respectively, is still rudimentary. Most of the work in this area has focused on mapping regions of the receptor responsible for drug binding affinity. Although binding of

ligand molecules to specific receptors represents the first event in the action of drugs, the efficacy with which this binding is translated into a physiological response remains the only determinant of therapeutic utility. In the last few years, increasing evidence suggested that receptor oligomerization and in particular dimerization may play an important role in the

5   molecular events leading to GPCR activation. In this paper, we review the biochemical and functional evidence supporting this notion.

PMID: 9666301

2.   Whitehead IP, Zohn IE, Der CJ. (2001) Rho GTPase-dependent transformation by G protein-coupled receptors. Oncogene 20: 1547-1555.

10   G protein coupled receptors (GPCRs) constitute the largest family of cell surface receptors, with more than 1000 members, and are responsible for converting a diverse array of extracellular stimuli into intracellular signaling events. Most members of the family have defined roles in intermediary metabolism and generally perform these functions in well-differentiated cells. However, there is an increasing awareness that some GPCRs can also

15   regulate proliferative signaling pathways and that chronic stimulation or mutational activation of receptors can lead to oncogenic transformation. Activating mutations in GPCRs are associated with several types of human tumors and some receptors exhibit potent oncogenic activity due to agonist overexpression. Additionally, expression screening analyses for novel oncogenes identified GPCRs whose expression causes the oncogenic transformation of

20   NIH3T3 mouse fibroblasts. These include Mas, G2A, and the PAR-1 thrombin receptor. In this review we summarize the signaling and transforming properties of these GPCR oncoproteins. What has emerged from these studies is the delineation of a GTPase cascade where transforming GPCRs cause aberrant growth regulation via activation of Rho family small GTPases.

25   PMID: 11313901

Panel 4.1D Summary: Ag1394 The GM563n7_A gene is expressed in normal kidney and is slightly induced in dermal fibroblasts after treatment with gamma interferon or IL-4. This observation suggests that the transcript encodes a putative GPCR that may be important in the normal function of the kidney and in the activation or response of dermal fibroblasts to Th1

30   or Th2 elaborated cytokines (gamma interferon and IL-4 respectively). Thus, expression of this gene could be used diagnostically to detect kidney tissue. Furthermore, the protein

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encoded for by the transcript could be used as a protein therapeutic to treat diseases of the skin, including psoriasis or allergy.

BU. GM656O22_B: GPCR

Expression of gene GM656o22_B was assessed using the primer-probe sets Ag1523 and Ag1898, described in Tables BUA and BUB. Results of the RTQ-PCR runs are shown in Tables BUC, BUD, BUE and BUF.

<u>Table BUA</u>. Probe Name Ag1523

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-agggcaagttcatagctctgtt-3'	22	860	555
Probe	TET-5'-ctacaccgtagtcactcctgcgctga-3'-TAMRA	26	882	556
Reverse	5'-cgtgttcctcagggtgtaaata-3'	22	915	557

<u>Table BUB</u>. Probe Name Ag1898

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ggctgtggtgtctctgtttttac-3'	22	786	558
Probe	TET-5'-catcttcatgtatctccagccagcca-3'-TAMRA	26	816	559
Reverse	5'-ctatgaacttgccctgctcat-3'	21	854	560

<u>Table BUC</u>. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1523, Run 142131146	Tissue Name	Rel. Exp.(%) Ag1523, Run 142131146
Endothelial cells	0.0	Renal ca. 786-0	0.0
Heart (Fetal)	0.0	Renal ca. A498	0.3
Pancreas	0.2	Renal ca. RXF 393	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. ACHN	0.0
Adrenal Gland	0.2	Renal ca. UO-31	0.3
Thyroid	0.0	Renal ca. TK-10	0.2
Salivary gland	0.2	Liver	0.0
Pituitary gland	0.0	Liver (fetal)	0.1

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Brain (fetal)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (whole)	0.0	Lung	0.0
Brain (amygdala)	0.1	Lung (fetal)	0.0
Brain (cerebellum)	2.0	Lung ca. (small cell) LX-1	0.1
Brain (hippocampus)	0.1	Lung ca. (small cell) NCI-H69	2.4
Brain (thalamus)	0.2	Lung ca. (s.cell var.) SHP-77	0.1
Cerebral Cortex	0.0	Lung ca. (large cell)NCI-H460	0.6
Spinal cord	0.0	Lung ca. (non-sm. cell) A549	1.0
glio/astro U87-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) HOP-62	0.6
astrocytoma SW1783	0.1	Lung ca. (non-s.cl) NCI-H522	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (squam.) SW 900	0.2
astrocytoma SF-539	0.0	Lung ca. (squam.) NCI-H596	1.0
astrocytoma SNB-75	0.2	Mammary gland	0.1
glioma SNB-19	0.4	Breast ca.* (pl.ef) MCF-7	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.1
glioma SF-295	0.0	Breast ca.* (pl. ef) T47D	0.6
Heart	0.3	Breast ca. BT-549	0.0
Skeletal Muscle	0.2	Breast ca. MDA-N	10.4
Bone marrow	0.2	Ovary	0.0
Thymus	0.0	Ovarian ca. OVCAR-3	0.0
Spleen	0.0	Ovarian ca. OVCAR-4	0.0
Lymph node	0.0	Ovarian ca. OVCAR-5	1.1
Colorectal Tissue	0.2	Ovarian ca. OVCAR-8	0.3
Stomach	0.0	Ovarian ca. IGROV-1	0.4

Small intestine	0.1	Ovarian ca. (ascites) SK-OV-3	0.4
Colon ca. SW480	0.0	Uterus	0.0
Colon ca.* SW620 (SW480 met)	0.0	Placenta	0.1
Colon ca. HT29	0.2	Prostate	19.3
Colon ca. HCT-116	0.0	Prostate ca.* (bone met) PC-3	0.3
Colon ca. CaCo-2	0.0	Testis	2.3
Colon ca. Tissue (ODO3866)	0.8	Melanoma Hs688(A).T	0.0
Colon ca. HCC-2998	0.0	Melanoma* (met) Hs688(B).T	0.4
Gastric ca.* (liver met) NCI-N87	0.1	Melanoma UACC-62	0.6
Bladder	0.5	Melanoma M14	4.1
Trachea	0.0	Melanoma LOX IMVI	0.2
Kidney	0.1	Melanoma* (met) SK-MEL-5	**100.0**
Kidney (fetal)	0.2		

Table BUD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1898, Run 165544705	Tissue Name	Rel. Exp.(%) Ag1898, Run 165544705
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	1.7	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	29.9	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	1.2	Lung ca. (small cell) LX-1	0.0

Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.3
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	2.6	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	4.1
Skeletal muscle	0.0	Ovary	0.8
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	1.3	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	2.2	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	4.2

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Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	31.9
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	2.3
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	6.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	**100.0**
Kidney	0.0	Adipose	0.0

Table BUE. Panel 2D

Tissue Name	Rel. Exp.(%) Ag1523, Run 145049949	Rel. Exp.(%) Ag1523, Run 145711220	Tissue Name	Rel. Exp.(%) Ag1523, Run 145049949	Rel. Exp.(%) Ag1523, Run 145711220
Normal Colon	5.2	0.0	Kidney Margin 8120608	0.0	0.0
CC Well to Mod Diff (ODO3866)	0.0	3.7	Kidney Cancer 8120613	0.0	0.0
CC Margin (ODO3866)	3.3	0.0	Kidney Margin 8120614	2.2	0.0
CC Gr.2 rectosigmoid (ODO3868)	0.0	0.0	Kidney Cancer 9010320	0.0	0.0
CC Margin (ODO3868)	0.0	4.2	Kidney Margin 9010321	0.0	0.0
CC Mod Diff (ODO3920)	0.0	0.0	Normal Uterus	0.0	0.0
CC Margin (ODO3920)	0.0	0.0	Uterus Cancer 064011	0.0	0.0
CC Gr.2 ascend colon (ODO3921)	2.0	0.0	Normal Thyroid	0.0	0.0
CC Margin	0.0	0.0	Thyroid	0.0	0.0

(ODO3921)			Cancer 064010		
CC from Partial Hepatectomy (ODO4309) Mets	0.0	0.0	Thyroid Cancer A302152	0.0	0.0
Liver Margin (ODO4309)	0.0	2.0	Thyroid Margin A302153	0.0	0.0
Colon mets to lung (OD04451-01)	0.0	0.0	Normal Breast	0.0	0.0
Lung Margin (OD04451-02)	0.0	0.0	Breast Cancer (OD04566)	0.0	0.0
Normal Prostate 6546-1	28.5	**100.0**	Breast Cancer (OD04590-01)	0.0	0.0
Prostate Cancer (OD04410)	**100.0**	56.3	Breast Cancer Mets (OD04590-03)	0.0	0.0
Prostate Margin (OD04410)	23.5	27.2	Breast Cancer Metastasis (OD04655-05)	0.0	0.0
Prostate Cancer (OD04720-01)	15.7	28.3	Breast Cancer 064006	0.5	0.0
Prostate Margin (OD04720-02)	11.7	11.2	Breast Cancer 1024	0.0	0.0
Normal Lung 061010	0.0	4.8	Breast Cancer 9100266	5.0	0.0
Lung Met to Muscle (ODO4286)	0.0	0.0	Breast Margin 9100265	1.8	2.9
Muscle Margin (ODO4286)	0.0	0.0	Breast Cancer A209073	3.1	0.0
Lung Malignant Cancer (OD03126)	8.2	5.3	Breast Margin A2090734	0.0	0.0
Lung Margin (OD03126)	0.0	0.0	Normal Liver	0.0	0.0
Lung Cancer (OD04404)	0.0	0.0	Liver Cancer 064003	1.8	5.4
Lung Margin (OD04404)	1.6	0.0	Liver Cancer 1025	0.0	0.0
Lung Cancer (OD04565)	0.0	0.0	Liver Cancer 1026	0.0	0.0
Lung Margin	0.0	0.0	Liver Cancer	0.0	0.0

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(OD04565)			6004-T		
Lung Cancer (OD04237-01)	0.0	0.0	Liver Tissue 6004-N	2.2	4.1
Lung Margin (OD04237-02)	0.0	0.0	Liver Cancer 6005-T	4.0	0.0
Ocular Mel Met to Liver (ODO4310)	2.5	2.7	Liver Tissue 6005-N	0.0	0.0
Liver Margin (ODO4310)	0.0	0.0	Normal Bladder	0.0	0.0
Melanoma Mets to Lung (OD04321)	3.6	0.0	Bladder Cancer 1023	0.0	0.0
Lung Margin (OD04321)	0.0	0.0	Bladder Cancer A302173	0.8	5.8
Normal Kidney	0.0	0.0	Bladder Cancer (OD04718-01)	0.0	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	0.0	Bladder Normal Adjacent (OD04718-03)	0.0	0.0
Kidney Margin (OD04338)	0.0	0.0	Normal Ovary	0.0	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	0.0	Ovarian Cancer 064008	0.0	0.0
Kidney Margin (OD04339)	0.0	0.0	Ovarian Cancer (OD04768-07)	0.0	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	0.0	Ovary Margin (OD04768-08)	0.0	0.0
Kidney Margin (OD04340)	0.0	0.0	Normal Stomach	0.0	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	0.0	Gastric Cancer 9060358	0.0	0.0
Kidney Margin (OD04348)	0.0	4.6	Stomach Margin 9060359	0.0	0.0
Kidney Cancer (OD04622-01)	0.0	0.0	Gastric Cancer 9060395	0.0	0.0
Kidney Margin	0.0	0.0	Stomach	3.7	0.0

(OD04622-03)			Margin 9060394		
Kidney Cancer (OD04450-01)	0.0	0.0	Gastric Cancer 9060397	0.0	0.0
Kidney Margin (OD04450-03)	0.0	0.0	Stomach Margin 9060396	0.0	0.0
Kidney Cancer 8120607	0.0	0.0	Gastric Cancer 064005	0.0	7.0

Table BUF. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1898, Run 164039381	Tissue Name	Rel. Exp.(%) Ag1898, Run 164039381
Secondary Th1 act	28.3	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	28.3	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0

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CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	19.2
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	99.3
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	26.2	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	26.8	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	**100.0**
Macrophages rest	0.0	Lung	58.6
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	84.1

HUVEC starved	0.0		

Panel 1.2 Summary: <u>Ag1523</u> Expression of the GM656o22_B gene is highest in a melanoma cancer cell line (CT=26.5), with expression detected in a cluster of melanoma cell lines. Thus, the expression of this gene could be used to distinguish samples derived from melanoma cell lines from other samples. In addition, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs or antibodies, might be of use in the treatment of melanoma. In addition, the GM656O22_B gene is expressed in healthy prostate tissue but not in the prostate cancer cell line.

The GM656O22_B gene is also expressed differentially in the cerebellum. Cerebellar G protein function is known to be defective in Alzheimer's disease cerebella, suggesting this cerebellum-preferential GPCR may have utility as a drug target to counter the G-protein signaling deficit in Alzheimer's disease.

<u>References:</u>

1. Fowler CJ, Garlind A, O'Neill C, Cowburn RF. (1996) Receptor-effector coupling dysfunctions in Alzheimer's disease. Ann N Y Acad Sci. 786:294-304.

There is now good evidence that in the AD brain, a number of neurotransmitter effector systems are defective. Such abnormalities include defective G, protein and protein kinase C function as well as a drastically reduced level of receptors for the second messenger Ins(1,4,5) P3. Such changes are probably not restricted to the late stages of the disease, and are found in regions of the brain that show little histopathological abnormality, such as the cerebellum. Whether these changes precede or are secondary to primary histopathological changes such as beta-amyloid deposition is not as yet clear. What is clear, however, is that such signal transduction abnormalities are likely to negate therapeutic benefits in clinical strategies based upon the tenet of neurotransmitter replacement.

PMID: 8687030

2. Cowburn RF, O'Neill C, Ravid R, Alafuzoff I, Winblad B, Fowler CJ. (1992) Adenylyl cyclase activity in postmortem human brain: evidence of altered G protein mediation in Alzheimer's disease. J Neurochem. 58:1409-19.

The effects of agonal status, postmortem delay, and age on human brain adenylyl cyclase activity were determined in membrane preparations of frontal cortex from a series of 18

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nondemented subjects who had died with no history of neurological or psychiatric disease. Basal and guanosine 5'-O-(3-thiotriphosphate)-, aluminum fluoride-, and forskolin-stimulated enzyme activities were not significantly reduced over an interval from death to postmortem of between 3 and 37 h and were also not significantly different between individuals dying with a long terminal phase of an illness and those dying suddenly. Basal and aluminum fluoride-stimulated enzyme activities showed a negative correlation with increasing age of the individual. In subsequent experiments, basal and guanosine 5'-O-(3-thiotriphosphate)-, aluminum fluoride-, and forskolin-stimulated enzyme activities were compared in five brain regions from a series of eight Alzheimer's disease and seven matched nondemented control subjects. No significant differences were observed between the groups for either basal activity or activities in response to forskolin stimulation of the catalytic subunit of the enzyme. In contrast, enzyme activities in response to stimulation with guanosine 5'-O-(3-thiotriphosphate) and aluminum fluoride were significantly reduced in preparations of neocortex and cerebellum from the Alzheimer's disease cases compared with the nondemented controls. Lower guanosine 5'-O-(3-thiotriphosphate)-, but not aluminum fluoride-, stimulated activity was also observed in preparations of frontal cortex from a group of four disease controls compared with nondemented control values. The disease control group, which contained Parkinson's disease and progressive supranuclear palsy patients, showed increased forskolin-stimulated activity compared with both the nondemented control and the Alzheimer's disease groups. These findings indicate a widespread impairment of G protein-stimulated adenylyl cyclase activity in Alzheimer's disease brain, which occurs in the absence of altered enzyme catalytic activity and which is unlikely to be the result of non-disease-related factors associated with the nature of terminal illness of individuals.

PMID: 1548475

Panel 1.3D Summary: Ag1898 Highest expression of the GM656O22_B gene is detected in a melanoma cell line (CT=31) as is seen in Panel 1.2, with low but significant expression also seen in the cerebellum and testis. Thus, the expression of this gene could be used to distinguish samples derived from this melanoma cell line from other samples. In addition, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs or antibodies, might be of use in the treatment of melanoma. Please see Panel 1.2 summary for potential relevance of expression in cerebellum to the treatment of CNS disorders.

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Panel 2D Summary: <u>Ag1523</u> Two experiments with the same probe and primer set show expression of the GM656O22_B gene to be highest in a normal prostate in one run and a prostate cancer in the second run. In addition, the expression seen in both runs on panel 2D is specific to prostate derived samples. Thus, expression of the GM656O22_B gene could be used to distinguish samples derived from prostate tissue from other samples. Furthermore, since there is substantial over expression observed in a sample derived from prostate cancer when compared to a sample derived from its normal adjacent tissue, therapeutic modulation of the expression or function of the GM656O22_B gene product, through the use of small molecule drugs or antibodies, may be useful in the treatment of prostate cancer. This observation is consistent with what is observed in Panel 1.2.

Panel 4D Summary: <u>Ag1898</u> Expression of this gene is low/undetectable (Ct values >35) in all samples on this panel (data not shown).

BV. GMAC009779_A/CG146581-01: Olfactory Receptor

Expression of gene GMAC009779_A (also known as CG146581-01) was assessed using the primer-probe set Ag1532, described in Table BVA. Results of the RTQ-PCR runs are shown in Tables BVB, BVC and BVD.

<u>Table BVA</u>. Probe Name Ag1532

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-ccttcttggaaatttccttcac-3'	22	213	561
Probe	TET-5'-tccaagggtcctgattagcatcacaa-3'-TAMRA	26	247	562
Reverse	5'-ccagcaaagctgatactcttgt-3'	22	279	563

<u>Table BVB</u>. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1532, Run 142232136	Tissue Name	Rel. Exp.(%) Ag1532, Run 142232136
Endothelial cells	0.0	Renal ca. 786-0	0.0
Heart (Fetal)	0.0	Renal ca. A498	0.4
Pancreas	0.0	Renal ca. RXF 393	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. ACHN	1.4

Adrenal Gland	0.0	Renal ca. UO-31	2.5
Thyroid	0.0	Renal ca. TK-10	0.6
Salivary gland	0.0	Liver	1.0
Pituitary gland	0.0	Liver (fetal)	0.0
Brain (fetal)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (whole)	0.0	Lung	0.0
Brain (amygdala)	0.0	Lung (fetal)	0.0
Brain (cerebellum)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (hippocampus)	0.0	Lung ca. (small cell) NCI-H69	22.2
Brain (thalamus)	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Cerebral Cortex	0.0	Lung ca. (large cell)NCI-H460	2.5
Spinal cord	0.0	Lung ca. (non-sm. cell) A549	3.0
glio/astro U87-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.8
glio/astro U-118-MG	0.6	Lung ca. (non-s.cell) HOP-62	7.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cl) NCI-H522	0.6
neuro*; met SK-N-AS	0.2	Lung ca. (squam.) SW 900	0.7
astrocytoma SF-539	0.3	Lung ca. (squam.) NCI-H596	5.5
astrocytoma SNB-75	0.6	Mammary gland	0.0
glioma SNB-19	2.9	Breast ca.* (pl.ef) MCF-7	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
glioma SF-295	0.0	Breast ca.* (pl. ef) T47D	7.7
Heart	**100.0**	Breast ca. BT-549	2.6
Skeletal Muscle	0.0	Breast ca. MDA-N	3.3
Bone marrow	0.7	Ovary	0.0
Thymus	0.0	Ovarian ca. OVCAR-3	1.3
Spleen	0.0	Ovarian ca. OVCAR-4	0.7
Lymph node	0.0	Ovarian ca. OVCAR-	20.0

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		5	
Colorectal Tissue	1.9	Ovarian ca. OVCAR-8	1.9
Stomach	0.0	Ovarian ca. IGROV-1	1.1
Small intestine	0.0	Ovarian ca. (ascites) SK-OV-3	1.0
Colon ca. SW480	0.0	Uterus	0.0
Colon ca.* SW620 (SW480 met)	0.0	Placenta	0.0
Colon ca. HT29	0.3	Prostate	0.0
Colon ca. HCT-116	0.0	Prostate ca.* (bone met) PC-3	1.2
Colon ca. CaCo-2	0.0	Testis	0.0
Colon ca. Tissue (ODO3866)	9.8	Melanoma Hs688(A).T	0.0
Colon ca. HCC-2998	1.2	Melanoma* (met) Hs688(B).T	2.7
Gastric ca.* (liver met) NCI-N87	0.6	Melanoma UACC-62	0.0
Bladder	4.3	Melanoma M14	7.3
Trachea	0.0	Melanoma LOX IMVI	0.0
Kidney	0.7	Melanoma* (met) SK-MEL-5	0.0
Kidney (fetal)	0.0		

Table BVC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1532, Run 148438266	Tissue Name	Rel. Exp.(%) Ag1532, Run 148438266
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca.	0.0

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		(hepatoblast) HepG2	
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
Glioma SNB-19	40.6	Mammary gland	0.0
Glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
Glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	85.3	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	**100.0**	Ovarian ca. IGROV-1	39.2

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Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table BVD. Panel 2D

Tissue Name	Rel. Exp.(%) Ag1532, Run 145030137	Rel. Exp.(%) Ag1532, Run 147317895	Tissue Name	Rel. Exp.(%) Ag1532, Run 145030137	Rel. Exp.(%) Ag1532, Run 147317895
Normal Colon	0.0	0.0	Kidney Margin 8120608	0.0	0.0
CC Well to Mod Diff (ODO3866)	23.2	**100.0**	Kidney Cancer 8120613	0.0	0.0
CC Margin (ODO3866)	0.0	**100.0**	Kidney Margin 8120614	0.0	0.0
CC Gr.2 rectosigmoid (ODO3868)	0.0	0.0	Kidney Cancer 9010320	0.0	0.0
CC Margin (ODO3868)	0.0	0.0	Kidney Margin 9010321	0.0	0.0
CC Mod Diff	59.5	53.6	Normal Uterus	0.0	0.0

(ODO3920)					
CC Margin (ODO3920)	0.0	0.0	Uterus Cancer 064011	0.0	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	0.0	Normal Thyroid	0.0	0.0
CC Margin (ODO3921)	13.8	10.4	Thyroid Cancer 064010	0.0	0.0
CC from Partial Hepatectomy (ODO4309) Mets	0.0	0.0	Thyroid Cancer A302152	0.0	0.0
Liver Margin (ODO4309)	0.0	0.0	Thyroid Margin A302153	0.0	0.0
Colon mets to lung (OD04451-01)	0.0	0.0	Normal Breast	0.0	0.0
Lung Margin (OD04451-02)	0.0	0.0	Breast Cancer (OD04566)	0.0	0.0
Normal Prostate 6546-1	0.0	0.0	Breast Cancer (OD04590-01)	0.0	0.0
Prostate Cancer (OD04410)	0.0	0.0	Breast Cancer Mets (OD04590-03)	0.0	0.0
Prostate Margin (OD04410)	0.0	0.0	Breast Cancer Metastasis (OD04655-05)	0.0	0.0
Prostate Cancer (OD04720-01)	0.0	0.0	Breast Cancer 064006	0.0	0.0
Prostate Margin (OD04720-02)	0.0	0.0	Breast Cancer 1024	0.0	0.0
Normal Lung 061010	0.0	0.0	Breast Cancer 9100266	0.0	0.0
Lung Met to Muscle (ODO4286)	0.0	16.7	Breast Margin 9100265	0.0	0.0
Muscle Margin (ODO4286)	0.0	0.0	Breast Cancer A209073	0.0	36.6
Lung Malignant Cancer (OD03126)	0.0	0.0	Breast Margin A2090734	0.0	0.0
Lung Margin (OD03126)	0.0	0.0	Normal Liver	0.0	0.0

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Lung Cancer (OD04404)	0.0	0.0	Liver Cancer 064003	20.0	21.5
Lung Margin (OD04404)	0.0	0.0	Liver Cancer 1025	0.0	0.0
Lung Cancer (OD04565)	0.0	0.0	Liver Cancer 1026	0.0	0.0
Lung Margin (OD04565)	0.0	0.0	Liver Cancer 6004-T	0.0	3.7
Lung Cancer (OD04237-01)	0.0	0.0	Liver Tissue 6004-N	16.8	18.8
Lung Margin (OD04237-02)	0.0	0.0	Liver Cancer 6005-T	0.0	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	0.0	Liver Tissue 6005-N	0.0	0.0
Liver Margin (ODO4310)	0.0	0.0	Normal Bladder	0.0	0.0
Melanoma Mets to Lung (OD04321)	0.0	0.0	Bladder Cancer 1023	0.0	0.0
Lung Margin (OD04321)	0.0	0.0	Bladder Cancer A302173	**100.0**	18.3
Normal Kidney	0.0	0.0	Bladder Cancer (OD04718-01)	0.0	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	37.6	Bladder Normal Adjacent (OD04718-03)	0.0	0.0
Kidney Margin (OD04338)	0.0	0.0	Normal Ovary	0.0	0.0
Kidney Ca Nuclear grade ½ (OD04339)	0.0	0.0	Ovarian Cancer 064008	0.0	0.0
Kidney Margin (OD04339)	0.0	0.0	Ovarian Cancer (OD04768-07)	0.0	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	0.0	Ovary Margin (OD04768-08)	0.0	0.0
Kidney Margin (OD04340)	0.0	0.0	Normal Stomach	0.0	0.0
Kidney Ca, Nuclear grade 3	0.0	18.6	Gastric Cancer 9060358	0.0	0.0

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(OD04348)					
Kidney Margin (OD04348)	0.0	21.6	Stomach Margin 9060359	0.0	0.0
Kidney Cancer (OD04622-01)	0.0	0.0	Gastric Cancer 9060395	0.0	0.0
Kidney Margin (OD04622-03)	0.0	0.0	Stomach Margin 9060394	0.0	0.0
Kidney Cancer (OD04450-01)	0.0	0.0	Gastric Cancer 9060397	0.0	0.0
Kidney Margin (OD04450-03)	0.0	0.0	Stomach Margin 9060396	0.0	0.0
Kidney Cancer 8120607	0.0	0.0	Gastric Cancer 064005	0.0	56.3

Panel 1.2 Summary: Ag1532 Expression of the GMAC009779_A gene is highest and almost exclusively restricted to heart muscle tissue (CT = 29.8). Thus, the expression of this gene could be used to distinguish heart muscle tissue from the other samples on this panel. Furthermore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies, or protein therapeutics, could be of use in the treatment of cardiovascular disease.

Panel 1.3D Summary: Ag1532 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2D Summary: Ag1532 The GMAC009779_A gene is expressed at highest levels in bladder cancer (CT=34.4) and a colon sample (CT = 34.8).

BW. GMAC026975_B/CG155797-01: Olfactory Receptor

Expression of gene GMAC026975_B (also known as CG155797-01) was assessed using the primer-probe set Ag2195, described in Table BWA. Results of the RTQ-PCR runs are shown in Table BWB.

Table BWA. Probe Name Ag2195

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Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-tctccttcatggagatctgcta-3'	22	254	564
Probe	TET-5'-ccaaactcatctcagatctgctggct-3'-TAMRA	26	293	565
Reverse	5'-cccaccaagatatgactttcct-3'	22	322	566

Table BWB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2195, Run 163630746	Tissue Name	Rel. Exp.(%) Ag2195, Run 163630746
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0

LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	12.9
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	11.8	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	10.7
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	12.4	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	10.2	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	23.0	Kidney	0.0
HUVEC starved	0.0		

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CNS_neurodegeneration_v1.0 Summary: <u>Ag2195</u> Expression of this gene is low/undetected (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: <u>Ag2195</u> Expression of this gene is low/undetected (CTs > 35) across all of the samples on this panel (data not shown).

5   **Panel 2D Summary:** <u>Ag2195</u> Expression of this gene is low/undetected (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: <u>Ag2195</u> Expression of the GMAC026975_B gene is only detected in liver cirrhosis (CT = 34.3). Furthermore, this transcript is not detected in normal liver in Panel 1.3D, suggesting that GMAC026975_B gene expression is unique to liver cirrhosis. 10   The GMAC026975_B gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

15   **BX. GM824K2_A: GPCR**

Expression of gene GM824k2_A was assessed using the primer-probe sets Ag2364 and Ag1725, described in Tables BXA and BXB. Results of the RTQ-PCR runs are shown in Tables BXC, BXD, BXE and BXF.

<u>Table BXA</u>. Probe Name Ag2364

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-caaccagccacagagatagttg-3'	22	289	567
Probe	TET-5'-cttcttgcaggaagccctccagcatt-3'-TAMRA	26	263	568
Reverse	5'-tctctacacctccgcagtgat-3'	21	236	569

20   <u>Table BXB</u>. Probe Name Ag1725

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-gctcaggtgacaactctcattc-3'	22	603	570

| Probe | TET-5'-tgtgttctgcctcactattccttttgga-3'-TAMRA | 28 | 629 | 571 |
| Reverse | 5'-caccacaattctggcataagat-3' | 22 | 668 | 572 |

Table BXC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2364, Run 208270664	Tissue Name	Rel. Exp.(%) Ag2364, Run 208270664
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	0.0
AD 2 Hippo	14.4	Control (Path) 4 Temporal Ctx	0.0
AD 3 Hippo	0.0	AD 1 Occipital Ctx	0.0
AD 4 Hippo	0.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	0.0	AD 3 Occipital Ctx	0.0
AD 6 Hippo	51.1	AD 4 Occipital Ctx	0.0
Control 2 Hippo	15.0	AD 5 Occipital Ctx	0.0
Control 4 Hippo	**100.0**	AD 6 Occipital Ctx	0.0
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	20.7	Control 2 Occipital Ctx	11.3
AD 2 Temporal Ctx	0.0	Control 3 Occipital Ctx	0.0
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	0.0	Control (Path) 1 Occipital Ctx	32.1
AD 5 Inf Temporal Ctx	0.0	Control (Path) 2 Occipital Ctx	0.0
AD 5 SupTemporal Ctx	0.0	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	0.0	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	0.0	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	0.0
Control 2 Temporal Ctx	0.0	Control 3 Parietal Ctx	46.3
Control 3 Temporal Ctx	0.0	Control (Path) 1 Parietal Ctx	25.2
Control 4 Temporal Ctx	0.0	Control (Path) 2 Parietal Ctx	0.0

Control (Path) 1 Temporal Ctx	0.0	Control (Path) 3 Parietal Ctx	45.4
Control (Path) 2 Temporal Ctx	0.0	Control (Path) 4 Parietal Ctx	0.0

Table BXD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2364, Run 165627930	Tissue Name	Rel. Exp.(%) Ag2364, Run 165627930
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	13.3	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
Glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
Glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	32.5
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.)	0.0

		NCI-H596	
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	86.5	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	28.1	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	56.3	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	100.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

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Table BXE. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag2364, Run 174553774	Tissue Name	Rel. Exp.(%) Ag2364, Run 174553774
Normal Colon	0.0	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	44.4
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Uterus	0.0
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer 064010	0.0
Prostate Margin (OD04410)	51.4	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer (OD04566)	49.7
Ovarian Cancer 064008	40.1	Breast Cancer 1024	0.0
Ovarian cancer	34.9	Breast Cancer	0.0

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(OD06145)		(OD04590-01)	
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis (OD04655-05)	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer 064006	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	0.0
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	0.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	82.4	Liver Tissue 6004-N	0.0
Ocular Melanoma Metastasis	0.0	Liver Cancer 6005-T	0.0
Ocular Melanoma Margin (Liver)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer 064003	0.0
Melanoma Margin (Lung)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer 1023	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer A302173	0.0
Kidney Margin (OD04338)	**100.0**	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0

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Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	74.7
Kidney Ca, Nuclear grade 3 (OD04348)	77.9	Gastric Cancer 064005	0.0

Table BXF. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1725, Run 165767161	Rel. Exp.(%) Ag2364, Run 162361133	Tissue Name	Rel. Exp.(%) Ag1725, Run 165767161	Rel. Exp.(%) Ag2364, Run 162361133
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	0.0
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	0.0	0.0
Secondary Tr1 act	0.0	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	0.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	0.0
Secondary Tr1 rest	2.1	0.0	Lung Microvascular EC none	2.3	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0	0.0
Primary Th1 rest	0.0	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	0.0	0.0	Small airway epithelium TNFalpha + IL-	0.0	0.0

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			1beta		
CD45RA CD4 lymphocyte act	0.0	0.0	Coronery artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8 lymphocyte rest	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0
Secondary CD8 lymphocyte act	0.0	0.0	KU-812 (Basophil) rest	0.0	13.0
CD4 lymphocyte none	0.0	0.0	KU-812 (Basophil) PMA/ionomycin	3.7	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	3.0	0.0
LAK cells IL-2	0.0	0.0	Liver cirrhosis	**100.0**	**100.0**
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	2.0	0.0
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+IL-18	0.0	0.0	NCI-H292 IL-4	0.0	0.0
LAK cells PMA/ionomycin	0.0	0.0	NCI-H292 IL-9	0.0	0.0
NK Cells IL-2 rest	0.0	0.0	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	0.0	NCI-H292 IFN gamma	0.0	0.0
Two Way MLR 5 day	0.0	0.0	HPAEC none	0.0	0.0
Two Way MLR 7 day	0.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	0.0
PBMC rest	0.0	0.0	Lung fibroblast none	0.0	0.0
PBMC PWM	0.0	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0

PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	0.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes CD40L and IL-4	0.0	0.0	Dermal fibroblast CCD1070 rest	0.0	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0
Dendritic cells none	0.0	0.0	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.0	12.0
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	6.3	20.7
Monocytes rest	0.0	0.0	IBD Crohn's	2.9	0.0
Monocytes LPS	0.0	0.0	Colon	9.7	0.0
Macrophages rest	0.0	0.0	Lung	0.0	0.0
Macrophages LPS	0.0	0.0	Thymus	0.0	25.3
HUVEC none	0.0	0.0	Kidney	0.0	0.0
HUVEC starved	4.5	0.0			

CNS_neurodegeneration_v1.0 Summary: Ag2364 Expression of the GM824k2_A gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag2364 Expression of the GM824k2_A gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5   **Panel 2.2 Summary:** Ag2364 Expression of the GM824k2_A gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag1725/Ag2364 The GM824k2_A transcript is only detected in liver cirrhosis. Furthermore, this transcript is not detected in normal liver in Panel 1.3D, suggesting that this gene expression is unique to liver cirrhosis. This gene encodes a putative

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GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

5   **BY. GMAP001804_C_1: GPCR**

Expression of gene GMAP001804_C_1 was assessed using the primer-probe set Ag1639, described in Table BYA. Results of the RTQ-PCR runs are shown in Tables BYB, BYC and BYD. Please note that this sequence was previously known as GMAP001804_C.

Table BYA. Probe Name Ag1639

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-agcatcttccacattgattcc-3'	21	693	573
Probe	TET-5'-cttcagcacctgcagctcccacataa-3'-TAMRA	26	734	574
Reverse	5'-ccaaagaacagagaaactgcaa-3'	22	760	575

10   Table BYB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1639, Run 165923902	Tissue Name	Rel. Exp.(%) Ag1639, Run 165923902
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	17.2
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	0.0	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0

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Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	6.7	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell)NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	10.6	Breast ca.* (pl.ef) MCF-7	15.2
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	25.7
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	**100.0**	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	6.6
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Plancenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0

Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	6.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	37.4
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table BYC. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag1639, Run 173978714	Tissue Name	Rel. Exp.(%) Ag1639, Run 173978714
Normal Colon	17.6	Kidney Margin (OD04348)	0.0
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	0.0
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-015)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	0.0

Colon mets to lung (OD04451-01)	0.0	Normal Uterus	16.6
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer 064010	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	0.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	0.0
Ovarian Margin (OD06283-07)	0.0	Breast Cancer (OD04566)	0.0
Ovarian Cancer 064008	**100.0**	Breast Cancer 1024	0.0
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	0.0
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis (OD04655-05)	0.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer 064006	0.0
Normal Lung	0.0	Breast Cancer 9100266	0.0
Invasive poor diff. lung adeno (ODO4945-01	17.1	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	0.0
Lung Malignant Cancer (OD03126)	0.0	Breast Margin A2090734	0.0
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	33.2
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	0.0
Lung Margin (OD05014B)	0.0	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin	0.0	Liver Tissue 6004-N	0.0

(OD04237-02)			
Ocular Melanoma Metastasis	0.0	Liver Cancer 6005-T	0.0
Ocular Melanoma Margin (Liver)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer 064003	72.7
Melanoma Margin (Lung)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer 1023	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer A302173	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Gastric Cancer 9060397	0.0
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	17.1
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table BYD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1639, Run 165762889	Tissue Name	Rel. Exp.(%) Ag1639, Run 165762889
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	3.8	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvasular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium	0.0

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		TNFalpha + IL1beta	
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	7.5
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	**100.0**
LAK cells IL-2+IL-12	0.0	Lupus kidney	3.4
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	3.6
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0

EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	11.7	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	18.6	IBD Colitis 2	26.1
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	61.6
Macrophages rest	4.2	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: <u>Ag1639</u> Expression of the GMAP001804_C_1 gene in this panel is highest in the spleen, an important site of secondary immune responses. Therefore, expression of this gene can be used to distinguish spleen from the other samples on this panel. Furthermore, antibodies or small molecule therapeutics that block the function of this GPCR may be useful as anti-inflammatory therapeutics for the treatment of allergies, autoimmune diseases, and inflammatory diseases. Expression is also detected at a much lower level in a melanoma and a breast cancer cell line.

Panel 2.2 Summary: <u>Ag1639</u> Significant expression of the GMAP001804_C_1 gene on panel 2.2 is restricted to one ovarian cancer and one liver cancer. This information suggests that this gene may be of use in the diagnosis and/or treatment of ovarian or liver cancer.

Panel 4D Summary: <u>Ag1639</u> The GMAP001804_C_1 transcript is expressed in IBD colitis, an activated basophil cell line and in dendritic cells. The protein encoded for by this gene may be important in the inflammatory process and particularly in the function of activated dendritic cells or basophils. Antagonistic antibodies or small molecule therapeutics against the GMAP001804_C_1 protein may therefore reduce or inhibit inflammation in the bowel due to IBD by specifically targeting dendritic cells and basophils or other related cell types. This gene was found to be expressed in spleen in Panel 1.3D.

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The GPCRX of this invention also encompasses the sequences of the SEQ ID NOS: 582, 583, 584, 585, 586, 587, 588 and 589 which can be found in Table 2.

Table 2

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC006313_B_amd	582/583	GGTCAAACTGCCCTTTACATCTCTCCCACTGCTTCTCCAAACCCTATCCAGGAA GTCCAGAGACATGGAGATAAAGAACTACAGCAGCAGCCACCTCAGGCTTCATCC TCCTGGGCCTCTCTTCCAACCCTCAGCTGCAGAAACCTCTCTTTGCCATCTTCCT CATCATGTACCTGCTCGCTGCCGGTGGGGAATGTGCTCATCATCCCGGCCATCTA CTCTGACCCCAGGCTCCACACCCCTATGTACTTTTTTCTCAGCAACTGTGTCTTTC ATGGATATCTGCTTCACAACAGTCATAGTGCCTAAGATGCTGGTGAATTTTCTA TCAGAGACAAAGGTTATCTCCTATGTGGGCTGCCTGGCCCAGATGTACTTCTTT ATGGCATTGGGAACACTGACAGCTACCTGCTGCTCTATGGCCATCGACCG GCTGGTGGCCATCTGCAACCCTTACACTATGATGTGGTTATGAAACCACGGC ATTGCCTGCTCATGCTATTGGGTTCTTGCAGCATCTCCCACCTACATTCCCGTGTT CCGCGTGCTACTTATGTCTCGCTGTTCTTTCGTGCCTCTCTGCCTCTGACACATCCTCC TTTTTCTGTGACACCCAGCCTGTGCTAAAGCTCCTCCTGCCTCTGACACATCCTCC AGCCAGATGGTGGTGATGACTGAGACCTTAGCTGTCATTGTGACCCCCTTCCTG TGTATCATCTTCTCTCACCTGCGAATCATGGTCACTGTGCTCAGAATCCCCTCT GCAGCCGGGAAGTGGAAGGCCTTCTCTACCTGTGGCTCCCACCTCACTGCAGT AGCCCTTTTCTATGGGAGTATTATTATGTCTATTTTAGGCCCCTGTCCATGTAC TCAGTGGTTAGGGACCGGGTAGCCACAGTTATGTACACAGTAGTGACACCCAT GCTGAACCCTTCATCTACAGCCTGAGGAACAAAGATATGAAGAGGGGTTTGA AGAAATTACAGGACAGAATTTACCGGTAAAAGGAACAAAATGTTG	MEIKNYSSSTSGFILLGLSS NPQLQKPLFAIFLIMYLLA AVGNVLIIPAIYSDPRLHT PMYFFLSNLSFMDICFTTV IVPKMLVNFLSETKVISYV GCLAQMYFFMAFGNTDS YLLASMAIDRLVAICNPLH YDVVMKPRHCLLMLLGS CSISHLHSLFRVLLMSRLS FCASHIIKHFFCDTQPVLK LSCSDTSSSQMVVMTETL AVIVTPFLCIIFSYLRIMVT VLRIPSAAGKWKAFSTCG SHLTAVALFYGSIYVYFR PLSMYSVVRDRVATVMY TVVTPMLNPFIYSLRNKD MKRGLKKLQDRIYR

Table 2

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC005962_B_amd	584/585	AAAACACCATGGAAAACAGGGAACCTCACGTGGGTATCAGAGACTTTGTCTTCCTG GGGCTCTCGCAGACTCGGGAGCTCCAGCGTTTCCTGTTTCTAATGTTCCTGTTT GTCTACATCACCACTGTTATGGGAAACATCCTTATCATCACAGTGACCTCT GATTCCCAGCTCCACACACCCATGTACTTTCTGCTCCGAAACCTGGCTGTCCTA GACCTCTGTTTCTTTCAGTCACTGCTCCCAAAATGCTAGTGGACCTCCTCTCT GAGAAGAAAACCATCTCTTACCAGGGCTGCATGGGTCAGATCTTCTTCTTCCAC TTTTTGGGAGGTGCCATGGTCTTCTTCCTCTCAGTGATGGCCTTTGACCGCCTC ATTGCCATCTCCCGGCCCCTCCGCCTATGTCACCGTCATGAACACTCAGCTCTGG GTGGGGCTGGTGGTAGCCACCTGGGTGGGAGGCTTTGTCCACTCTATTGTCCA GCTGGCTCTGATGCTCCCACTGCCCTTCTGTGGCCCCAACATTTTGGATAACTT CTACTGTGATGTTCCCCAAGTACTGAGACTTGCCTGCACTGACACCTCACTGCT GGAGTTCCTCAAGATCTCCAACAGTGGGCTGCTGGATGTCGTCGGTTCTTCCT CCTCCTGATGTCCTACTTATTCATCCTGGTGATGCTGAGGTCACATCCAGGGGA GGCAAGAAGGAAGGCAGCTTCCACCTGCCACCACCACATCATCGTGGTTTCCA TGATCTTCGTTCCAAGCATTTACCTCTATGCCCGGCCCTTCACTCCATTCCCTAT GGACAAGCTTGTGTCCATCGGCCACAGTCATGAGCCCCATGCTCAACCCCAT GATCTATACCCTGAGGAACCAGGACATGCAGGCAGCAGTGAGAAGATTAGGG AGACACCGGCTGGTTTGAGA	METGNLTWVSDFVFLGLS QTRELQRFLMFLFVYIT TVMGNILIITVTSDSQLHT PMYFLLRNLAVLDLCFSS VTAPKMLVDLLSEKKTIS YQGCMGQIFFHFLGGAM VFFLSVMAFDRLIAISRPL RYVTVMNTQLWVGLVVA TWVGGFVHSIVQLALMLP LPFCGPNILDNFYCDVPQV LRLACTDTSLLEFLKISNS GLLDVVWFFLLLMSYLFIL VMLRSHPGEARRKAASTC TTHIIVVSMIFVPSIYLYAR PFTPFPMDKLVSIGHTVM TPMLNPMIYTLRNQDMQ AAVRRLGRHRLV

Table 2

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAC009642_C_amd	586/587	AAATCATGACTTTGGTTTCTTTTTTCTTTTCCTCTCCAAGCCATTGATAATGCT CCTTAGCAATTCAAGCTGGAGGCTATCCCAGCCTTCTTTTCTCCTGGTAGGGAT TCCAGGTTTAGAGGAAAGCCAGCACTGGATTGCACTGCCCCTGGGCATCCTTT ACCTCCTTGCTTTAGTGGGCAATGTTACCATTCTCTTCATCATCTGGATGGACC CATCCTTGCACCAATCTATGTACCTCTTCCTGTCCATGCTAGCTGCCATCGACC TGGTTCTGGCCTCCTCCACTGCACCCAAAGCCCTTGCAGTGCTCCTGGTTCATG CCCACGAGATTGGGTACATCGTCTCGTCCTGATCCAGATGTTCTTCATCCATGCAT TCTCCTCCATGGAGTCAGGGGTACTTGTGGGCCATGGCTCTGGATCGCTATGTGTAG CCATTTGTCACCCCTTGCACCATTCCACAATCCTGCATCCAGGGGTCATAGGGC GCATCGGAATGGTGGTGCTGGTGAGGGGATTACTACTCCTTATCCCCTTCCCCA TTTTGTTGGGAACACTTATCTTCTGCCAAGCCACCATCATAGGCCATGCCTATT GTGAACATATGGGCTGACTATGCCCCACATCCTCCAGGCAGTGCTGAAGGTACCAGGGAGTGA GCTTATGGGCTGACTGTGTTGTGAAACTTGCCTGCTCAGAAACCACAGTCAATCGA GGTGTTTCCTATGCCCACATCCTCCAGGCAGTGCTGAAGGTACCAGGGAGTGA GGCCCGACTTAAGGCGTTAGCACATGTGGCTCTCATATTTGTGTCATCCTGGT CTTCTATGTCCCTGGAATTTTCTCCTTCTCCACTCACCGCTTTGGTCATCATGTA CCCCATCATGTCCATGTTCTATGGAGTGAAGACTCAGCAGATCCGCCAGCGAGTGCTCTC CTCAATCCTCTTGTCTATGGAGTGAAGACTGATCTGAACATATTCTCATT AGAGTGTTTACACAAAAGGATTGATCTGAACATATTCTCATT	MTLVSFFSFLSKPLIMLLS NSSWRLSQPSFLLVGIPGL EESQHWIALPLGILYLLAL VGNVTILFIIWMDPSLHQS MYLFLSMLAAIDLVLASS TAPKALAVLLVHAHEIGYI VCLIQMFFIHAFSSMESGV LVAMALDRYVAICHPLHH STILHPGVIGRIGMVVLVR GLLLIPFPILLGTLIFCQA TIIGHAYCEHMAVVKLAC SETTVNRAYGLTMALLVI GLDVLAIGVSYAHILQAV LKVPGSEARLKAFSTCGS HICVILVFYVPGIFSFLTHR FGHHVPHHVHVLLATRYL LMPPALNPLVYGVKTQQI RQRVLRVFTQKD

Table 2

Acc. No.	SEQ ID NO (Nucl) / SEQ ID NO (Prot)	DNA SEQUENCE	PROTEIN SEQUENCE
GMAP000818_D_amd	588/589	CCATGAGGAATTTCTCGGTGGTGTCCGAATTCATCCTGCTGGGCATCCCTCACA CGGAGGGTCTGGAGACTATTCTGTTGGTCCTGTTTTTGTCCTTCTACATCTTCA CCCTTATGGGGAACCTGCTCATCTTGCTGGCTATTGTCTCCTCTGCTCGGCTTC ACACGCCCATGTACTTCTTCCTGTGCAAGCTGTCTGTTTTTGACCTATTTTTCCC TTCTGTGAGTTCCCCTAAGATGCTGTGCTATCTTTCAGGGAACAGCCGAGCCAT CTCCTATGCAGGCTGTGCATCCCAGCTCTTCTTCTACCATTTCCTGGGCTGCAC TGAGTGTTTCCTGTACACGGTGATGGCCTACGACCGCTTTGTTGCCATTTGTCA CCCTCTACGCTACACCATAATCATGAGCCACAGAGCATGTATCATCCTAGCCAT GGGGACCTCATTCTTTGGCTGCATTCAGGCACCTTTCTGACCACTCTCACCTT CCAATTGCCTTACTGTGTCCCCAATGAGGTGGACTATTATTTCTGTGATATCCC AGTCATGCTGAAGCTGGCTTGTGCAGATACCTCAGCGCCCTGGAGATGGTGGGGT TCATCAGTGTGGGCCTCATGCCCCTCAGCTGTTCCTTCTCATCCTCACCTCCTA CAGTGGCATCGTCTTCTCCATCTTGGAGATCTGCTCTGCGGAGGCCGACGCCG TGCCTTCTCCACCTGCAGCGCCTGCCACCTCACCGCCATCCTGCTTTTTACATGCC AGTGGTCCTCATTTACCTGAGGCCTACCCACAGCCTGTGGTTGGATGCAACTGT TCAAATTCTGAATAACCTGGTCACCCCATGCTGAACCCCTTAATCTACAGTCT CAGGAATAAGGAGGTGAAATTATCACTAAGGAAGGTCTTATATCAGCTGGGCT TCCTTCCTGAGCAGTTGTAGAGAGAAATAA	MRNFSVVSEFILLGIPHTE GLETILLVLFLSFYIFTLMG NLLILLAIVSSARLHTPMY FFLCKLSVFDLFFPSVSSPK MLCYLSGNSRAISYAGCA SQLFFYHFLGCTECFLYTV MAYDRFVAICHPLRYTIIM SHRACIILAMGTSFFGCIQ ATFLTLTFQLPYCVPNEV DYYFCDIPVMLKLACADT SALEMVGFISVGLMPLSCF LLILTSYSGIVFSILEICSAE GRRRAFSTCSAHLTAILF YMPVVLIYLRPTHSLWLD ATVQILNNLVTPMLNPLIY SLRNKEVKLSLRKVLYQL GFLPEQL

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OTHER EMBODIMENTS

Although particular embodiments have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims, which follow. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the invention without departing from the spirit and scope of the invention as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims.